The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

Vol. 142, No. 11 — Chicago, Illinois — March 18, 1950
Copyright, 1950, by American Medical Association

ROENTGEN EXAMINATION OF THE CHEST

Its Limitations in the Diagnosis of Disease

LEO G. RIGLER, M.D.
Minneapolis

A consideration of the possibilities and limitations of roentgen examination in the diagnosis of chest conditions is, in effect, an effort to estimate the value of the roentgen method. Such a consideration must begin with a division of roentgen findings into those which lead to the detection of an abnormal process and those which lead to the identification of the nature of the lesion. While in some situations the discovery of an abnormality in the roentgenogram may carry with it an almost certain determination of its etiology, more commonly identification must rest on more elaborate studies with the use of numerous other diagnostic methods.

It is in the discovery of lesions that the roentgen examination has its greatest usefulness and likewise its greatest reliability. With the rapid advancement in the technic of roentgenography, the utilization of mass surveys, and the widespread recognition of the necessity for roentgen study of all patients with suspected intrathoracic disease, there has come about a degree of reliance on the roentgen examination for the detection of disease which may not be completely justified. If an abnormal condition is shown in the roentgenogram, its clinical significance can usually be determined by appropriate studies. But what is the significance of a normal roentgenogram? That question is far more difficult to answer. Furthermore, the answer may well be different for each disease.

It is evident that the determination of the limitations of the roentgen detection of disease, which is, in effect, a determination of the significance of the normal roentgenogram, must be measured in certain terms of reference. The most important of these is time. Summers [1] has aptly said that time might well be considered a fourth dimension in the determination of the significance of roentgen findings. The time of invasion of an infection or of the inception of a neoplasm would be the best points of reference. Since both of these are frequently unknown, the time of onset of symptoms may well be used. While it is obvious that some time must elapse after the inception of a disease process before abnormal conditions become apparent in the roentgenogram, the same is not true if the onset of symptoms is used as a point of reference. Here the variation of time in different disease conditions may be considerable: in some cases the roentgen findings precede the onset of symptoms; in others the interval before the appearance of changes is short, while in others a long delay may occur between the development of clinical findings and the roentgenographic evidence of abnormality. In certain situations, of course, there are never any abnormal roentgen signs.

Second, the size of the lesion may be used as a point of reference. It is possible, in some instances at least, to determine the minimum size necessary for roentgen demonstration. In effect, this represents a size permitting distinction from the normal pattern of the lung. Finally, one should consider the time relationship of the first evidences of disease shown in the roentgenogram to the first physical signs which become apparent.

Data which bear on these questions are difficult to collect, since these points of reference are often not sharp and are frequently difficult to determine. My associates and I have made some studies, however, both on animals and on clinical cases which give pertinent information, some of which will be summarized here. I propose to indicate the value of the normal roentgenogram in the diagnosis of a specific number of intrathoracic diseases selected because they illustrate both the advantages and disadvantages of roentgen study and because we have been able to collect data bearing on them.

Relatively little has been written about this problem, although as a practical matter it is of great moment. Brailsford [2] has discussed it to some degree, and publications by Dale,[3] McPhedran,[4] Axen [5] and others have dealt with it in various phases. I have previously elaborated on this thesis with specific case reports.[6]

PULMONARY EDEMA

One of the simplest of the abnormal processes affecting the lungs is pulmonary edema. Here the exudation of fluid into the alveoli produces striking and rapid changes in the roentgenogram. The determination of the time of inception of the condition is only occasionally possible. The onset of symptoms is seldom sharp enough to be reliable. Some evidence can be gleaned by roentgen examination of patients undergoing surgical intervention on the thorax. In some of these, by reason of malposition of the patient and deviations of the mediastinum, localized pulmonary edema may occur. Roentgenograms made at operation reveal that within a few minutes after the earliest possible inception of such a process definite changes in the lung of significant degree can be observed. This is true of obstructive atelectasis also, but the changes are not so

From the Department of Radiology and Physical Medicine, University of Minnesota.

Read before the Section on Diseases of the Chest at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1949.

1. Summers, J.: Personal communication to the author.

2. Brailsford, J. F.: Proc. Royal Soc. Med. **38**: 555, 1945; Radiology **46**: 184, 1946; Practitioner **157**: 200, 1946.

3. Dale, T.: Acta radiol., supp. 16, pp. 1-111, 1932.

4. McPhedran, F. M.: Am. J. Med. Sc. **173**: 245, 1927; Am. Rev. Tuberc. **16**: 420 and 479, 1927. McPhedran, F. M., and Weyl, C.: Am. J. Med. Sc. **173**: 313, 1927.

5. Axen, O.: Acta radiol. **22**: 547, 1941.

6. Rigler, L. G., and Exner, F. B.: Latent Period in Roentgen Diagnosis of Pulmonary Tuberculosis: Preliminary Report, J. A. M. A. **102**: 1750 (May 26) 1934. Rigler, L. G.: Am. J. Roentgenol. **61**: 743, 1949.

rapidly apparent. Clinical cases of pulmonary edema as a result of cardiac failure, overloading of the circulation after operative procedure, renal conditions, hypoproteinemia of various origins and a variety of other causes have been studied. From these studies it is clear that signs of pulmonary edema may be evident roentgenographically before the patient is fully conscious of any abnormality or within an hour or two after the first onset of dyspnea. Furthermore, roentgen signs are clearly visible in all cases well before, as long as twelve hours before, physical changes are noted.

There are a few striking exceptions to the dictum that pulmonary edema can be observed with extreme rapidity after its onset. Such exceptions appear to occur when the edema is interstitial rather than intra-alveolar. This type of edema may be the first indication of an inflammatory process in the lungs but may also occur in the first stages of other types of edema. Under these circumstances, while some changes in the roentgenogram may become apparent, they are not at all clearcut and, therefore, are difficult to diagnose. In some animal experiments we have found that interstitial edema may be of sufficient degree to give severe symptoms without obvious roentgen signs.

PNEUMONIA

A similar difference exists in the determination of the presence of pneumonia. Interstitial lesions, such as occur in so-called atypical, or virus, pneumonia and as a result of various other organisms, are manifested in the roentgenogram only at an extremely late stage. In most instances, twenty-four to forty-eight hours must elapse after the onset of symptoms before the development of any characteristic signs in the roentgenogram representing these types of pneumonia. It is true that the physical signs in such cases are even more delayed, and commonly the roentgen findings are clearly apparent well before the onset of any physical manifestations. But the roentgen findings follow the symptoms by fairly long periods of time in the interstitial types of pneumonia.

The converse is true in the bacterial lobar pneumonias, in which, even in the early stages, there is rapid exudation of fluid into the alveoli. In a fairly large series of cases we have been able to observe definite evidences of pneumonia in the roentgenogram in as short a time as an hour and a half after the onset of detectable symptoms and in almost all cases within twelve hours after such onset. We had 2 cases in which fortuitous circumstances permitted the observation of the patients within a short time after a sharp onset of symptoms of typical bacterial lobar pneumonia. The time at which roentgen changes were apparent was one and one-half and two hours, respectively, after the onset of symptoms; a much larger number of cases in which changes became apparent at six, seven and eight hours have also been observed. In many of these physical examination also had begun to give indications of the existence of an abnormal process, although at this stage they were indistinct and indefinite, while the roentgen findings were already distinctive.

Thus a normal roentgenogram is of relatively little significance during the first forty-eight hours after the appearance of symptoms suggestive of atypical pneumonia or other nonbacterial pneumonias. On the other hand, a normal roentgenogram observed more than twelve hours after the onset of symptoms thought to be due to bacterial pneumonia speaks strongly against the presence of such a process and should induce study of other organs to determine the source of the symptoms.

PLEURAL LESIONS

The limitations of roentgen diagnosis in diseases of the chest are well illustrated in the case of pleural lesions. In the majority of cases in which acute pleurisy occurs without exudation of fluid, the roentgen findings may appear to be almost normal or may be extremely difficult to elicit. It is true that there may be some elevation and immobility of the diaphragm on the side of involvement, but in many instances even this sign is not apparent, although the patient definitely has acute pleurisy. With the onset of fluid in the pleural cavity, the roentgen findings may not be clearly apparent in the earliest stages of the exudation. This is particularly true if the roentgen examination, whether it be radiographic or fluoroscopic, is not made in a variety of positions, particularly in the supine and lateral decubitus positions. In the average adult as much as 300 cc. of fluid may be present in the pleural cavity without giving obvious evidences in the usual upright posteroanterior roentgenogram; even in the lateral view this much fluid may not be clearly visible. The addition of a roentgenogram made with the patient in the the lateral decubitus position, as described many years ago,[7] will make evident much smaller amounts of fluid. Experiments on animals, with recalculation in terms of the volume of the adult human thorax, indicate that as small an amount as 100 cc. of fluid in either pleural cavity will be visible under these circumstances. We have repeatedly demonstrated, in persons with an acute attack of pain and fever, small amounts of fluid in the inferior costal gutter by making a posteroanterior roentgenogram with the patient lying on the side of the lesion, although in the usual upright position no evidence whatever of the fluid could be discovered. Physical examination and fluoroscopic study commonly show some diminution in the motion of the diaphragm.

PULMONARY TUBERCULOSIS

That pulmonary tuberculosis can be detected roentgenographically early in its development, well before the onset of symptoms or of physical signs, is well established. It is important, however, to determine just how early is the stage of development at which roentgen findings become apparent. This is particularly important now that large numbers of apparently normal persons are being examined to determine the presence of tuberculosis, either in the course of routine surveys or because of contact with tuberculous patients in one way or another. Among hospital personnel, particularly among medical students and nurses, unwitting exposures to tuberculosis occur frequently and are discovered often within a relatively short time after the exposure has taken place. After such a discovery, roentgenograms of the chest are commonly made as soon as possible. At such a time a perfectly clear and normal roentgenogram may give a false sense of security, for it has been well demonstrated by many studies that at least eight weeks, and more likely ten weeks at the minimum, must elapse after the ordinary type of exposure to tuberculosis before the development of any roentgen signs can possibly be determined.

The time which must elapse before the roentgen findings become apparent will depend largely on the location of the lesion and its size. While experimentally, in the phantom, shadows as small as 2 mm. in diameter are demonstrable in the roentgenogram, in the average adult this is scarcely possible. With such relatively solid tissues as metastases, lesions as

7. Rigler, L. G.: Roentgen Diagnosis of Small Pleural Effusions: A New Roentgenographic Position, J. A. M. A. **96**: 104 (Jan. 10) 1931.

small as 3 mm. in diameter may well be distinguished from the surrounding vascular trunks and other normal structures of the lung. In tuberculosis, the detection of a lesion of such small size is even more difficult, since the process is usually not uniform or dense in its beginning. An appreciable time passes, therefore, between the development of the first microscopic tubercles and their advance to a sufficient size so that they are visible. Fortunately, most tuberculosis of this type occurs moderately well out in the periphery of the lung so that it is readily visible, even in small size. Nevertheless, at least eight weeks, and more likely ten weeks, must elapse after the introduction of the infection before the abnormal conditions become apparent. In many instances an even longer period of time than ten weeks must be considered, possibly as long as twenty weeks, before the normal roentgenogram can be considered to be of great significance.

It is obvious that this latent period in the development of the roentgen findings is of great significance in the estimation of the results of survey examinations or of the observation of contacts in cases of tuberculosis, since in a small percentage of these it is possible that the roentgen examination may be made exactly during this latent period. The delay in the development of roentgen signs may account, in part at least, for the cases of tuberculosis which were discovered among Army personnel shortly after an apparently normal roentgenogram had been made at the induction center.

Occasionally the roentgenogram appears to show normal conditions even after the development of a substantial lesion. These are rare and represent instances in which the lesion is hidden in the relatively invisible areas of the lung, such as the portion below the dome of the diaphragm, behind the heart and overlying the mediastinum. If elaborate examinations which include oblique views, lateral views and lordotic views were made in every case, even these lesions would be more uniformly discovered. As a practical matter, however, it is not feasible to make such elaborate examinations in what are presumably normal persons, since the productivity is relatively low. However, when there is the slightest suspicion of the presence of a real lesion, on the basis of symptoms or other highly suggestive evidence, such elaborate examinations should be undertaken in order to determine the presence of the disease at an early stage.

It should be noted that, in occasional cases, bronchial tuberculosis occurs without any apparent parenchymal extension in its early stages. Under such circumstances it is possible that the sputum may even be positive without any evidence in the roentgenogram of an abnormality in the lungs. These cases are rare, but they do occur and should be borne in mind.

In pulmonary tuberculosis, which is acquired in the normal manner or by endogenous reinfection, it may therefore be said that abnormal conditions will be evident roentgenographically almost always within ten to twenty weeks after the exposure or the inception of the lesion. If symptoms suggestive of ordinary pulmonary tuberculosis are present, a normal roentgenogram, with rare exceptions, tends to rule out pulmonary tuberculosis as a cause of the symptoms. In the absence of symptoms, however, the latent period in the development of roentgen signs makes the normal roentgenogram of less significance.

In miliary tuberculosis, the results of roentgen examination are completely different. The roentgen signs of miliary tuberculosis invariably follow rather than precede the onset of symptoms. There is a great variation in the time of development of roentgen signs in acute miliary tuberculosis. In many instances the changes may be observed within a week or ten days after the onset of symptoms; in others they are far more delayed. It is our opinion that this is largely a function of the number and size of the miliary tubercles. It is not uncommon to find numerous miliary tubercles, particularly along the pleural surfaces, at autopsy, without any roentgen evidence whatever. We have observed patients who had characteristic symptoms, which were proved by the eventual results to be due to acute miliary tuberculosis, for as long as seven weeks without the roentgenographic observation of any abnormality in the lungs whatever, although the patient died of the disease eventually. In these instances the tubercles are usually small, less than 1 mm. in diameter, and not sufficiently numerous so that the accidental superimposition of a number of these lesions would produce roentgenographic changes.

In experiments conducted on adults, we have found that a 1 mm. lesion by itself, when located on the chest wall, even in close juxtaposition to the film, is not distinguishable in the ordinary roentgenogram. However, three or four such 1 mm. pieces of tissue superimposed on each other, even at some distance apart, will produce a faint shadow. Such data has already been accumulated by Axen,[5] Dale,[3] McPhedran[4] and others. It is evident, therefore, that the normal roentgenogram in acute miliary tuberculosis, even long after the onset of symptoms, is of no significance.

METASTASES

It is in the demonstration of nodular lesions, such as metastases, that the roentgen examination exhibits its most startling accuracy, for here the lesions are invariably obvious in the roentgenogram long before the onset of symptoms and long before the appearance of physical signs. Despite this, lesions smaller than 3 mm. are usually not distinguishable. Furthermore, larger lesions, up to 8 mm. in diameter, may well be present without being obvious in the roentgenogram unless oblique or lateral views are made in addition to the usual posteroanterior views. We have observed 1 case of metastasis from a Ewing's tumor over a period of several years, during which individual small lesions have appeared in both lungs. These were segmentally resected on five occasions. During the course of the observation of this case we were able to see lesions of approximately 3 mm. in diameter sufficiently well to differentiate them from the ordinary vascular shadows. Lesions larger than 3 mm. in diameter were easily determined. Nevertheless, some lesions as large as 8 mm. in diameter were completely overlooked in the ordinary posteroanterior roentgenogram because of superimposition on structures well out at the axilla, behind the heart and over the diaphragm, although they became perfectly visible as soon as repeated examination was made in a variety of positions.

Metastases of the miliary type may also be completely invisible in the roentgenogram when they are present in insufficient number or are of small size. We have been able to demonstrate this on a number of occasions when normal roentgenograms have been made just prior to surgical exploration or autopsy. In these cases miliary metastases were observed by the surgeon or pathologist and confirmed microscopically. Therefore, a normal roentgenogram in these instances is not conclusive evidence of the absence of metastases, since, if less than 2 mm. in diameter or if miliary in size and not numerous, they may not be visible.

Finally, I should like to summarize the evidence concerning the possibilities and limitations of the roentgen method in the detection of bronchogenic carcinoma. It should be emphasized again that this discussion concerns itself with the detection of an abnormality shown by the roentgenogram, which should lead to further study eventuating in the diagnosis of primary carcinoma of the lung, rather than the roentgen identification of the disease. The latter can be accomplished in some instances by elaborate roentgen study, but more frequently a definitive diagnosis must be established by microscopic observation. The increasing frequency with which carcinoma of the lung is seen and the unfortunate fact that the vast majority of patients are still observed in the late stages raises questions as to the best procedure for the early detection of such lesions.

Can abnormal conditions be seen in the roentgenogram before the onset of symptoms in bronchogenic carcinoma, and are roentgen findings always abnormal in the presence of symptoms of bronchogenic carcinoma? To answer these two questions it seems desirable to divide the cases into two general groups. In the first group there are the peripheral, usually nodular and almost invariably nonobstructive lesions, which are the less common of the bronchogenic carcinomas but the most readily observable roentgenographically. In this group the lesion is invariably obvious roentgenographically before the onset of symptoms or physical signs. Such peripheral carcinomas not infrequently are found during the course of mass chest surveys. Many of these lesions are slow-growing; a study of a series of cases shows the presence in the roentgenogram of shadows in the periphery of the lung as long as seven years before the development of an obvious symptomatic carcinoma in 1 case and two to three years in a fairly large number of cases. Unfortunately, it is in this group that the greatest difficulty occurs in the definitive diagnosis of carcinoma, and frequently only exploratory surgical procedures can be relied on to make the distinction between carcinoma and other more benign processes. It is clear, however, that in the peripheral lesions there are roentgen findings long before the onset of symptoms or physical signs.

In the majority of cases of bronchogenic carcinoma the lesions are more central and involve some bronchial obstruction. In rare cases symptomatic evidence of a carcinoma of the bronchus may well be present without the appearance of any abnormal conditions in the ordinary roentgenogram. Such symptoms as hemoptysis, slight wheezing, cough or pain may well occur at a time when the lesion is confined to the bronchial lumen and is yet insufficiently developed to produce any of the obvious obstructive signs. If roentgenograms of such patients were made in expiration as well as in inspiration at this stage, it is possible that the evidences of an obstructive emphysema might well be found. This might lead, therefore, to further investigation, and the diagnosis might be established at an early stage. In a number of cases in which the patient had symptoms, we have demonstrated obstructive emphysema in the expiratory film, although the usual roentgenogram appeared to be normal. On the other hand, in some of these, films made in expiration also may not reveal the evidence of any obstruction, the lesion being so small that it does not produce even an obstructive emphysema, although cough and hemoptysis might occur from superficial ulceration of the tumor. Such cases are undoubtedly rare.

COMMENT

We have studied a large number of cases in which symptoms were present and roentgen findings apparently absent. In almost every instance the discrepancy is explained either by incomplete examination or by failure to interpret abnormal changes properly. The most common error in interpretation occurs as a result of insufficient attention to moderate, unilateral enlargement of the hilar shadow of the lung. This may be an early sign of carcinoma of the lung and is commonly present well before the patient has any obvious clinical signs.

A second common error lies in the failure to observe minor degrees of differences in the radiability of segments or larger portions of the lung. Early in the stage of carcinoma of the lung, emphysema may be present. While this is much more prominent in expiration, it may also be observed in inspiration in many cases and may be the first evidences of the lesion. We have observed cases in which emphysema preceded other symptoms by one and a half to two years.

In other instances, linear atelectasis may be an early sign, only a small segment of the lung being involved and contracting down to such a degree that it produces a relatively minor shadow which is easily overlooked. This may be present before the onset of symptoms or may be the only evidence apparent in the roentgenogram at the time when symptoms are already present.

In occasional instances extremely small infiltrations in the lung are present but lie so close to the root shadow that in the ordinary film they are mistaken for vascular trunks. In such situations the roentgen findings may appear to be absent, although the patient already has cough, pain in the chest and even hemoptysis. Again, more careful attention to minor changes in the linear markings of the lung would indicate the presence of a pathologic process and stimulate further investigation.

Our studies have indicated that in the vast majority of cases involving central as well as peripheral tumors roentgen evidences are apparent before the onset of symptoms. Furthermore, in only rare instances has there been a complete absence of roentgen evidences of abnormality when the symptoms were already present. Two cases recently reported in the literature as contravening this dictum both showed clear signs of abnormality, unilateral emphysema in 1 case and enlarged hilar shadow in the other, conditions which had obviously been overlooked at the original interpretation.

In order to establish such minor conditions it is necessary to make careful and critical study of every roentgenogram of the chest. Furthermore, in many cases, multiple views in addition to the usual posteroanterior upright film made in inspiration are imperative. Especially is it important to have films made in expiration and in the oblique positions. In the presence of symptoms such maneuvers should always be undertaken. It is questionable, however, whether it would be feasible to make such elaborate studies in ordinary surveys of presumably well persons. Further studies are now being conducted to determine whether the productivity of such an elaborate examination is sufficient to justify its use as a routine survey method even among persons in the age group in which cancer is most prevalent.

In the presence of symptoms of bronchogenic carcinoma, therefore, the normal roentgenogram is of great significance, especially if a complete study has been made and careful interpretation has been given.

SUMMARY

A consideration of the significance of the normal roentgenogram in the diagnosis of a number of intrathoracic lesions based on experimental and clinical observation gives rise to the following conclusions:

1. Pulmonary edema can be detected before the onset of appreciable symptoms or within a few hours thereafter. It is detectable in the roentgenogram from six to twelve hours before the appearance of physical signs.

2. Pleural effusion in amounts of 100 cc. or more can be detected if proper technic is used.

3. Bacterial pneumonias give evidences in as short a time as two hours, most frequently within six hours and almost invariably within twelve hours of the onset of definite symptoms.

4. Atypical or virus pneumonias may give no distinctive roentgen findings for twenty-four to forty-eight hours after the onset of symptoms.

5. Pulmonary tuberculosis of the ordinary chronic type is not demonstrable until eight to twenty weeks after the exposure.

6. Acute miliary tuberculosis invariably produces symptoms before the development of roentgen signs. The latter may not be present for as long as seven weeks after the onset of symptoms.

7. Nodular lesions such as those produced by metastasis or nodular tuberculosis are demonstrable when their size is 3 mm. or larger in diameter. Even lesions of this size will not be seen if multiple films in various positions are not made or if the lesions are unfavorably located.

8. Metastases of miliary size, such as those produced by miliary tuberculosis, may not be visible until numerous or large in size.

9. All metastases are roentgenographically visible before the onset of symptoms or physical signs.

10. Bronchogenic carcinoma almost invariably gives positive roentgen signs when symptoms are present, if thorough examination is done. There are a few exceptions to this rule. In most instances, roentgen evidences of abnormality will be present before the onset of any respiratory symptoms due to bronchogenic carcinoma. Complete examination is necessary, however, to establish these evidences.

ABSTRACT OF DISCUSSION

DR. LAWRENCE L. ROBBINS, Boston: The points which Dr. Rigler has brought out are extremely important and are frequently overlooked. In the past, it has been said that it is relatively easy to determine the presence of disease by means of a roentgenogram of the chest. I think that physicians will agree, after hearing Dr. Rigler, that this is not easy in many instances. It may be impossible to reach an accurate diagnosis, even with the closest study and cooperation between clinician and radiologist, and this is particularly true in some cases of early diffuse lesions and small round lesions within the lung. It is assumed that excellent technic and all the ramifications of methods of technic have been utilized. Even so, my associates and I have had an embarrassing period in the last few years, in which over 50 patients with chronic tuberculosis have undergone surgical procedures, either lobectomy or pneumonectomy. The major portion of the disease was readily recognized but, to our chagrin, there were multiple lesions scattered throughout the remainder of the lungs or lobes which were unrecognizable, even in retrospect. So, we have come to feel that a roentgen examination which shows normal conditions has the limitations which Dr. Rigler has pointed out. I believe that patients are coming to physicians earlier with bronchial carcinoma, and it may be only through extremely careful examination that they will be able to locate the lesion. We have recently had cases in which the results of cytologic examinations were positive, and it was only with extreme difficulty that we made a diagnosis. In one instance, a small lesion on the posterior wall of the right main bronchus was readily overlooked by the bronchoscopist and was not clearly demonstrable on the films. It was only after about two months' observation that it was possible to locate the lesion, either by radiologic methods or by bronchoscopic examination; the patient then underwent surgical intervention. The shape of the lesion, of course, is oftentimes of particular importance in the diagnosis, and here multiple views as well as fluoroscopic examination are extremely valuable. The value of repeated examinations cannot be stressed too much. Physicians are all aware that carcinoma of the lung is often first called atypical pneumonia and that it is only by following the average case of pneumonia through to its clearing that one is able to know that it is a pneumonic process. Round shadows are frequently observed, and it must be decided whether they represent tumors of a malignant or a benign nature. We have had the unfortunate experience recently of watching 2 patients over a period of approximately two years and then finding that the lesions were inoperable carcinomas. Consequently, we have come to believe that radical surgical procedures are of extreme value in these cases of unknown lesions so that the cases of early carcinoma can be salvaged. There are numerous possibilities and numerous limitations in roentgenographic diagnosis. It is extremely important to improve radiographic technic, to obtain an even closer relationship between the radiologist and the clinician and to know the natural history of the disease much better than it is known at present.

DR. PHILIP J. HODES, Philadelphia: To me, as a radiologist, the most interesting portions of Dr. Rigler's paper were those that concerned the limitations of roentgen technics in the diagnosis of diseases of the chest. Nothing is more unsatisfactory to a radiologist than to have to render a report of normal conditions on the chest of a patient who obviously has clinical symptoms. And nothing is more frustrating to the radiologist than the history of hemoptysis when, radiographically, the patient's chest looks normal. Yet this is by no means a unique experience. In some ways it is a healthy experience, because it dispels smugness and keeps reminding radiologists of their limitations. However, the implications are far different for the referring physician because, unless he realizes the limitations of the radiologist, he will be lulled into a false sense of security by a report of normal conditions, to the detriment of his patient. The history and the clinical findings still are, and probably always will be, the indispensible factor in the patient's clinical history, and no radiologist's report of normal conditions should be allowed to replace them unless enough time has been allowed to elapse and unless the radiologist has examined the chest time and time again. The reasons for this discrepancy are simple and have already been mentioned by Dr. Rigler and Dr. Robbins. Briefly, they include the size of the lesion, which is of prime importance, the size of the chest around the lesion, which is probably related to the size of the lesion, and the pneumatization of the lung around the lesion. The position of the lesion, as Dr. Rigler demonstrated, is extremely important in its recognition. Finally, the actual ventilation of the lung itself will determine whether or not a great many lesions will be seen. I would like to ask Dr. Rigler if, in his experiments, he has resorted to body section technics to test the lesions that he sees in routine roentgenograms. It has been our experience that the body section films probably show the lesion in its truer size, since it usually appears larger in the body section film than it does in the routine study.

DR. LEO G. RIGLER, Minneapolis: This discussion added much to what I had to say. I purposely omitted any reference to technic or reliability of interpretation because what I had in mind really were the physical limits of the method rather than its utilization, which is, of course, as variable as the persons who apply it. My associates and I use body section radiology commonly in detection of lesions, and we are occasionally able to see lesions with body section that we are unable to see otherwise. However, so far as size is concerned, I have never made any experiments with that particularly in mind.

STEROIDS IN THE TREATMENT OF EARLY PREGNANCY COMPLICATIONS

M. EDWARD DAVIS, M.D.
and
NICHOLAS W. FUGO, Ph.D.
Chicago

Endocrine therapy in early pregnancy to prevent and to combat the hazard of abortion has never been used more extensively than at present. In one clinic use of small or large amounts of estrogens is advocated prophylactically and in the treatment of threatened abortions; in another, varying amounts of progesterone are administered, and in a third clinic a combination of progesterone and estrogens has been most effective.[1] In some of the studies, steroid hormones have not been used but emphasis has been placed on the careful management of the patient, diet, increased intake of vitamin E, vitamin K or ascorbic acid, and thyroid. In these current reports the results of varying therapeutic regimens do not differ greatly. Somewhere in this bizarre clinical picture there must be a pattern for an intelligent approach in the treatment of conditions that may cause abortion. The present study has been undertaken to provide some additional factual knowledge so that eventually a scientific basis for the treatment of early pregnancy complications can be developed.

Pregnancy may not progress normally for many reasons. Heuser, Rock and Hertig[2] have demonstrated that some pregnancies fail prior to implantation because of an abnormal ovum or sperm. Other pregnancies reach the implantation stage, but their normal growth is thwarted by defective germ plasm or an abnormal environment inimical to continued survival. The frequency of abortions due to these factors is difficult to ascertain, but some evidence is available in a report by Wall and Hertig,[3] who studied a group of women with habitual abortion, that 58 per cent repeated abortion on the same etiologic basis. Of these abortions, 43 per cent were caused by ovular factors and 15 per cent by maternal factors. Normal development of pregnancy is dependent on the hormonal support provided by estrogens and progesterone as well as on other glandular substances. Early in the gestation the corpus luteum is the chief source of these steroids. However, toward the end of the first trimester the placenta takes over their production. It is entirely possible, in rare instances, to dispense with the corpus luteum as early in the pregnancy as six weeks and have the pregnancy continue uneventfully.

Failure in the hormonal support for the pregnancy may stem primarily from a defective trophoblast, in which case insufficient chorionic gonadotropin is available to maintain corpus luteum activity; this results in inadequate amounts of estrogens and progesterone early in the pregnancy, when they are essential for implantation, vascularization and growth. It may result from primary corpus luteum failure in spite of adequate gonadotropic stimulation. Hormonal support may be adequate early in the pregnancy, but waning corpus luteum activity may not be compensated by increasing placental function as this structure assumes the responsibility for steroid production.

The recent report of Delfs and Jones[4] emphasized the importance of deviations in the normal hormonal pattern. Thus, they observed that low levels of chorionic gonadotropin were associated with a pathologic conceptus and were always followed by abortion. Early low pregnanediol excretion was often associated with low chorionic gonadotropin levels. It is not possible to ascertain in many of these cases whether we are dealing with primary failure of hormonal support because of glandular inadequacy or failure secondary to a defective trophoblast. Theoretically, many of these failures, early and late, could be corrected by the administration of estrogens and progesterone.

Major emphasis has been placed on progesterone in the establishment and maintenance of normal pregnancy. This hormonal substance is largely responsible for decidual development, implantation and early growth changes. In conjunction with estrogens, it projects the growth of the endometrium beyond the premenstrual phase and complements estrogens in the vascularization so necessary for the development of the placenta. Marrian[5] and Venning and Browne[6] have elucidated the metabolism of progesterone, and Venning has described a method for the quantitative determination of sodium pregnanediol glucuronidate, an inert metabolic product, in the urine.[7] It is possible to follow progesterone metabolism in the menstrual cycle and in pregnancy by determining the amount of urinary pregnanediol by the Venning method or by a method which we described previously.[8]

Methods for studying estrogen metabolism are less satisfactory, so much work remains to be done in determining the complete history of the hormonal changes in normal and abnormal pregnancy.

The discovery of estrogenic substances and their ready availability as natural and synthetic preparations prompted clinicians to use them extensively for the prevention and treatment of abortion. Karnaky in 1942[9] suggested the use of large doses of diethylstilbestrol, orally and in the cervix, in order to stay the process of threatened or inevitable abortion. However, the work of the Smiths[10] on the metabolism of steroids in normal pregnancy and its complications is responsible for the present widespread use of diethylstilbestrol in early and late pregnancy complications.

In 1936 the Smiths[11] observed that in normal

Dr. Edward Henderson and the Schering Corporation supplied the crystalline progesterone (prolution®) used in this study.

Read before the Section on Obstetrics and Gynecology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

This work was done under a grant from the Douglas Smith Foundation for Medical Research and the Joseph Bolivar DeLee Research Fund of the University of Chicago.

From the Department of Obstetrics and Gynecology and the Department of Pharmacology, the University of Chicago School of Medicine and the Chicago Lying-in Hospital.

1. Vaux, N. W., and Rakoff, A. E.: Estrogen-Progesterone Therapy: A New Approach in the Treatment of Habitual Abortion, Am. J. Obst. & Gynec. **50**: 354, 1945.
2. Heuser, C. H.; Rock, J., and Hertig, A. T.: Carnegie Institution of Washington Publication no. 557, 1945, p. 85.
3. Wall, R. L., Jr., and Hertig, A. T.: Habitual Abortion, Am. J. Obst. & Gynec. **56**: 1127, 1948.
4. Delfs, E., and Jones, G. E. S.: Endocrine Patterns in Abortion, Obst. & Gynec. Surv. **3**: 680, 1948.
5. Marrian, G. F.: Observations on the Chemical Nature of Crystalline Oestrin, J. Soc. Chem. Ind. **49**: 515, 1930.
6. Venning, E. H., and Browne, J. S. L.: A Study of the Metabolism of Crystalline Progesterone, Endocrinology **27**: 707, 1940.
7. Venning, E. H.: Gravimetric Method for the Determination of Sodium Pregnanediol Glucuronidate, J. Biol. Chem. **119**: 473, 1937.
8. Davis, M. E., and Fugo, N. W.: A Simplified Method for the Quantitative Determinations on Free Pregnanediol Excretion in Pregnancy, Soc. Exper. Biol. & Med. **66**: 39, 1947.
9. Karnaky, K. J.: The Use of Stilbestrol for the Treatment of Threatened and Habitual Abortion and Premature Labor: A Preliminary Report, South. M. J. **35**: 838, 1942.
10. Smith, G. V. S., and Smith, O. W.: Internal Secretions and Toxemia of Late Pregnancy, Physiol. Rev. **28**: 1, 1948.
11. Smith, G. V., and Smith, O. W.: The Urinary Excretion of Estrogenic and Gonadotropic Hormones During Menstrual Cycles, The Period of Conception and Early Pregnancy, New England J. Med. **215**: 908, 1936.

pregnancy there is a decided rise in estrogen secretion at ten or twelve weeks, when there is a simultaneous drop in chorionic gonadotropin levels. This rise in estrogen level is preceded by an increased secretion of progesterone. They concluded that estrogens utilize chorionic gonadotropin for the placental production of progesterone. In 1941 [12] they presented additional data to support the theory that estrogen oxidation products rather than estrogens are responsible for the progesterone-stimulating effects of estrogens on the placenta. They subsequently suggested that diethylstilbestrol specifically, not because of its estrogenic effect, stimulates the placental syncytium to produce estrogens and progesterone by the utilization of chorionic gonadotropin.

The Smiths and Hurwitz [13] administered diethylstilbestrol to a diabetic patient who was pregnant and noted that the amount of pregnanediol in the urine increased. Cessation of therapy was followed by a drop in urinary pregnanediol, and on the resumption of treatment with diethylstilbestrol the output again increased. This provided clinical confirmation for the work of the Smiths and led them to recommend the administration of graduated amounts of diethylstilbestrol to pregnant patients in order to prevent and to decrease the hazards of early and late pregnancy complications.

MATERIAL AND METHOD

Patients who had repeated (habitual) abortions were selected for this study. The reports of Malpas,[14] Eastman [15] and others have indicated that the term "habitual aborter" should be reserved for the woman who has had at least three consecutive pregnancies which terminated spontaneously during the previable stage. Statistically, the likelihood of a subsequent untreated pregnancy ending in the delivery of a viable infant is about one in six, or 16 per cent. These women were studied thoroughly to determine the normalcy of their reproductive organs, their general physical status, glandular function and other pertinent data. Basal metabolic rates and seminal fluid studies were made on the husbands. The Rh factor was determined in the patient and her husband. Our own experience confirms that of Hunt [16] and others, who could not demonstrate any relation between habitual abortion and erythroblastosis. However, Potter in our clinic has observed that an abortion may sensitize a mother occasionally so that she may later give birth to an infant with erythoblastosis.

These patients were advised to report soon after the missed menstrual period. The basal temperature record and the Friedman test were used to establish the diagnosis of pregnancy in most women. Patients were given routine antepartum care customary at the Chicago Lying-in Hospital. Additional instructions consisted in abstinence from coitus and douches and travel beyond 50 miles (80.5 kilometers). Many of these patients made daily visits to the hospital, which necessitated long rides in automobiles or public conveyances.

The women were instructed in the collection of twenty-four hour urine specimens, which they brought to the laboratory two or three times each week. Creatinine determinations were used as a check on the completeness of each collection. After the first or second urine collection, to establish a base line, each patient in group 1 was given 50 mg. of diethylstilbestrol orally each day. No other medication was prescribed. All urine samples were examined quantitatively for free pregnanediol by a method that we described previously. Chorionic gonadotropin and estrogen assays were made at least once a week in each patient. Patients in group 2 were treated similarly, but in place of diethylstilbestrol progesterone was administered intramuscularly, usually at daily intervals; no less than 300 mg. was given per week. Some patients who were treated with diethylstilbestrol in one pregnancy, which ended in abortion, were treated with progesterone in the next pregnancy. Most of the women tolerated the daily parenteral injections, consisting of 50 mg. of progesterone in 1 cc. of oil. In a few instances some local induration developed because of the slow absorption of the oil.

TABLE 1.—*Results in Women with Habitual Abortion Treated with Diethylstilbestrol*

	Patients	Pregnancies	Living Infants	Percentage
Past history.....	38	174	15	8.5
Pregnancy under study.....	38	42	19	45.2

TABLE 2.—*Results in Women with Habitual Abortion Treated with Progesterone*

	Patients	Pregnancies	Living Infants	Percentage
Past history.....	18	75	8	10.7
Pregnancy under study.....	18	18	12	66.7

RESULTS

In table 1 are summarized the results of the treatment of 38 women having habitual abortion with large doses of diethylstilbestrol. Prior to this study the women had a total of 174 pregnancies and only 15 living infants, a fetal salvage of 8.5 per cent. The group was followed in 42 pregnancies which resulted in 19 living infants, a fetal salvage of 45.2 per cent.

These results do not compare favorably with many similar groups reported in the literature in recent years, in which women were treated by a variety of regimens. Most of the authors report more than a 50 per cent salvage. As an example, Delfs and Jones [17] were able to deliver 29 living infants in 43 pregnancies which were carefully studied and in which thyroid insufficiency was the most frequent observation. They administered thyroid, oral progesterone or vitamin E to those patients in whom these substances were considered deficient. Javert reported an 80 per cent salvage in patients with primary habitual abortion.[18] The treatment consisted of nutritional instructions, dietary supplements, including ascorbic acid and vitamin K, with thyroid when indicated. They noted that the elimination of vitamins E and K and of progesterone produced no evident reduction in full term fetal salvage. Smith, in a recent report on the use of diethylstilbestrol

12. Smith, O. W.; Smith, G. V. S., and Schiller, S.: Estrogen and Progestin Metabolism in Pregnancy: I. Spontaneous and Induced Labor, J. Clin. Endocrinol. **1**: 461, 1941.
13. Smith, O. W.; Smith, G. V., and Hurwitz, D.: Increased Excretion of Pregnanediol in Pregnancy from Diethylstilbestrol with Special Reference to the Prevention of Late Pregnancy Accidents, Am. J. Obst. & Gynec. **51**: 411, 1946.
14. Malpas, P.: Study of Abortion Sequences, J. Obst. & Gynaec. Brit. Emp. **45**: 932, 1938.
15. Eastman, N. J.: Habitual Abortion, in Progress in Gynecology, New York, Grune & Stratton, Inc., 1946.
16. Hunt, A. B.: The Rh Factor in Abortion, Am. J. Obst. & Gynec. **53**: 467, 1947.
17. Delfs, E., and Jones, G. E. S.: Some Aspects of Habitual Abortion, South. M. J. **41**: 809, 1948.
18. Javert, C. T.: Habitual Abortion, New York State J. M. **48**: 2595, 1948.

by a number of clinicians, reported that of 41 women who had three previous abortions 80 per cent gave birth to living children, and of 29 who had four previous abortions 52 per cent had live births.

In table 2 are summarized the results of the treatment of 18 women having habitual abortion with large

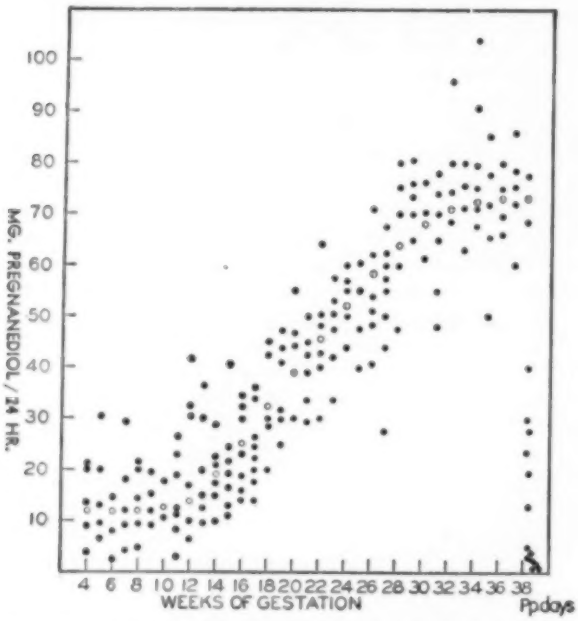


Fig. 1.—Excretion of pregnanediol in a group of patients during normal pregnancy and the immediate postpartum period.

doses of progesterone. The past histories of these women revealed that they had a total of 75 pregnancies, only 8 (10.7 per cent) of which resulted in living children. Twelve living children were born to these 18 women who were treated during their current

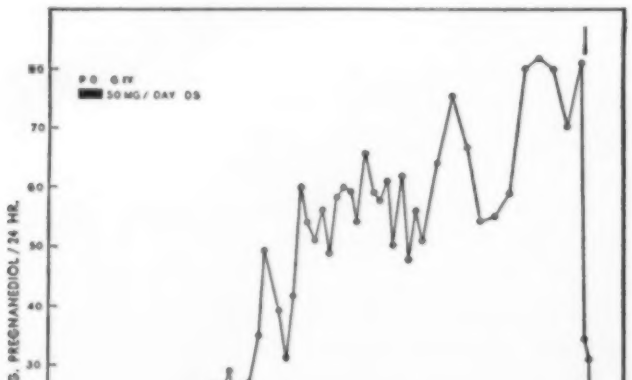


Fig. 2.—Pregnanediol excretion in patient receiving 50 mg. of diethylstilbestrol daily who had uneventful pregnancy and living infant. In this and succeeding illustrations DS denotes diethylstilbestrol; P O G IV indicates the number of the parity (0) and gravidity (4).

pregnancies, a fetal salvage of 66.7 per cent. It is noteworthy that diethylstilbestrol was administered to half of these women in one or more previous pregnancies which ended in abortion.

A number of different patterns were observed in the study of these patients. Figure 1 is a composite curve demonstrating the excretion of pregnanediol in a group of patients during normal pregnancy and the immediate postpartum period. Note the characteristic low level of pregnanediol excreted during the first twelve to fourteen weeks of the gestation, the gradual rise as pregnancy advances and the precipitate drop following delivery.

Figures 2 and 3 represent the curves of pregnanediol excretion in 2 patients who had uneventful pregnancies and deliveries of living infants. The first patient received 50 mg. of diethylstilbestrol daily and the second, 100 mg. In figure 2 the corpus luteum phase of progesterone secretion is supplemented by the syncytial phase at about ten or twelve weeks. In figure 3 this transition occurred at about fifteen weeks. The quantity of diethylstilbestrol administered daily did not appear to influence the excretion of free pregnanediol, for the levels in the patient receiving 100 mg. of the drug were somewhat lower than those in the woman consuming 50 mg. daily. Progesterone therapy produced no evident reduction in full term fetal salvage.

Mrs. G. (fig. 4) had five pregnancies which terminated in abortion, the majority in the first trimester. In her sixth pregnancy, 100 mg. of diethylstilbestrol was administered daily. This pregnancy (upper portion fig. 4) terminated at

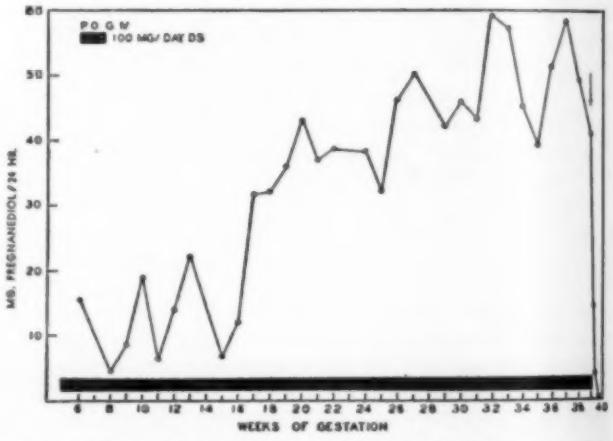


Fig. 3.—Pregnanediol excretion in patient receiving 100 mg. of diethylstilbestrol daily who had uneventful pregnancy and living infant.

the end of the first trimester. In the seventh pregnancy the daily intake of diethylstilbestrol was reduced to 75 mg. This gestation progressed to about the seventeenth week. The placental phase of progesterone production was not apparent in the curve (lower portion of fig. 4).

It is probable that a recurrent factor or factors were responsible for the failure of seven consecutive pregnancies to go to a successful conclusion. It is equally evident that the administration of diethylstilbestrol did not stimulate the production of additional hormonal support to make the continuation of the gestation possible.

Mrs. A. (fig. 5), a diabetic patient, had three previous abortions at twenty-four to twenty-six weeks. Her diabetes was controlled with some difficulty. She received 50 mg. of diethylstilbestrol daily. Only small amounts of free pregnanediol were excreted during the first 18 weeks of the gestation, at which time the pregnancy was regarded as lost. This was followed by a transient spurt of progesterone metabolism, which rapidly sank again to low levels. At twenty-four weeks the patient gave birth to a fetus evidently dead for about one week. This sudden increase in the free pregnanediol titer was obviously placental in origin, but this structure must have been inadequate to provide continued hormonal support.

Mrs. P. (fig. 6) had a living baby, after which five pregnancies terminated late in the second trimester. In the seventh pregnancy 50 mg. of diethylstilbestrol was administered daily.

The corpus luteum phase of progesterone metabolism was erratic, no pregnanediol being excreted on some days. At about fourteen weeks there was a rise in free pregnanediol, and because this level was maintained it was assumed that placental production of progesterone would maintain the pregnancy. At twenty-four weeks the patient went into labor and delivered a normal previable fetus.

Mrs. W. (fig. 7) had two previous pregnancies which terminated late in the second trimester. She received 25 mg. of diethylstilbestrol daily immediately after the missed menstrual period. The level of free pregnanediol was so low that when she was nine weeks pregnant the dose of diethylstilbestrol was increased to 50 mg. daily. At twenty weeks there was no improvement, and the pregnancy, was regarded as lost. Fifty milligrams of progesterone in oil was injected daily in addition to the orally administered diethylstilbestrol. The prompt improvement in the level of free pregnanediol was greater than could be accounted for by the injected progesterone. She gave birth to a normal living previable fetus at twenty-five or twenty-six weeks. Grossly and histologically, the placenta was normal.

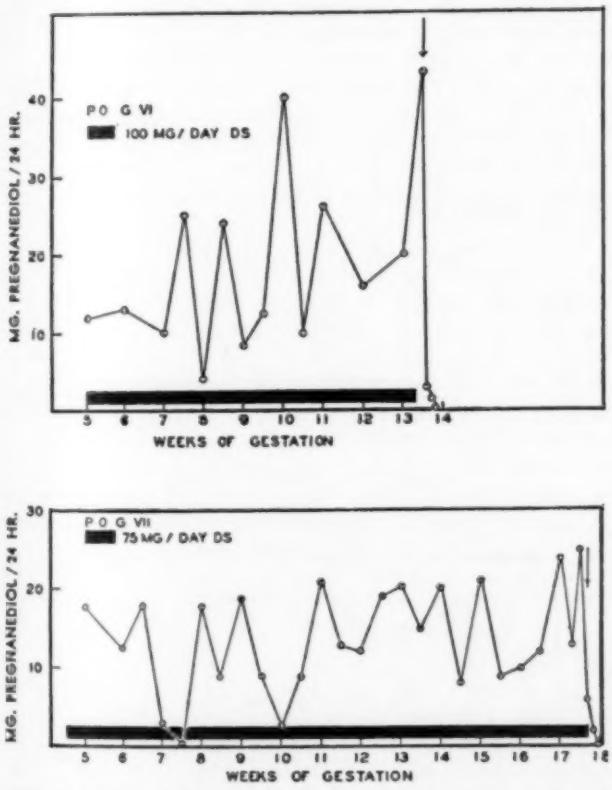


Fig. 4.—Pregnanediol excretion in sixth pregnancy of patient receiving 100 mg. of diethylstilbestrol daily (upper portion) and in seventh pregnancy of same patient receiving 75 mg. of diethylstilbestrol daily (lower portion).

In the 3 preceding patients (figs. 5, 6 and 7) the site of failure of hormonal support must have been the corpus luteum. This may have been brought about by a deficient chorion so that too little chorionic gonadotropin was available for corpus luteum maintenance. It could have been the result of primary corpus luteum failure. The hormonal deficiency continued into the placental phase in 2 of the patients, which would provide further proof of a deficient chorion. Apparently diethylstilbestrol did not influence the corpus luteum phase of steroid production, nor did it provide a sufficient stimulus for syncytial steroid production. Is it possible that the early administration of ample amounts of progesterone may have substituted for an ineffective corpus luteum and improved the prognosis for their pregnancies?

Mrs. S. had five previous pregnancies, all of which ended in abortion. Figure 8 is a record of three pregnancies followed in the present study. In her sixth pregnancy (top curve) she received 50 mg. of diethylstilbestrol daily. Pregnanediol levels were normal for the corpus luteum phase, but she aborted at about thirteen weeks. The same plan of treatment was followed in the seventh pregnancy.

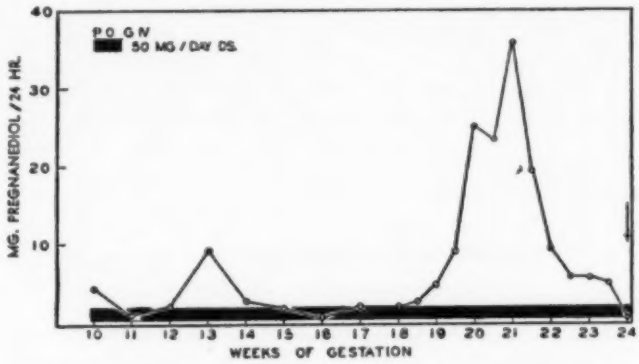


Fig. 5.—Pregnanediol excretion of pregnant diabetic patient receiving 50 mg. of diethylstilbestrol daily.

This gestation continued for twenty weeks, when she gave birth to a normal previable fetus (middle curve). Pregnanediol levels remained rather stationary throughout the course of the pregnancy. The syncytial phase of steroid production is not manifest in this curve.

In her eighth pregnancy 50 mg. of progesterone were administered daily. The curve (bottom portion of fig. 8) of

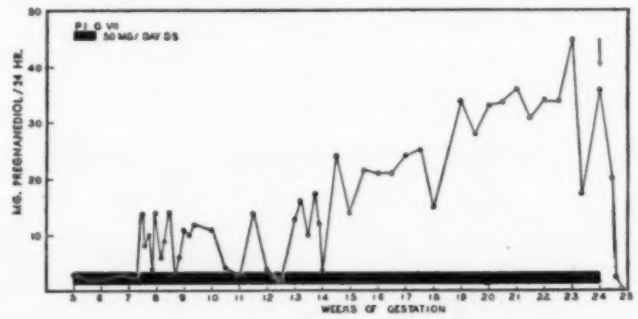


Fig. 6.—Pregnanediol excretion in seventh pregnancy of patient receiving 50 mg. of diethylstilbestrol daily.

pregnanediol excretion did not vary greatly from the preceding one, although the general level was slightly higher, probably because of the metabolism of the ingested progesterone. This pregnancy terminated at about twenty weeks. It is possible that there is a recurrent inherent trophoblastic defect. Neither diethylstilbestrol nor progesterone altered the unfavorable course of these pregnancies.

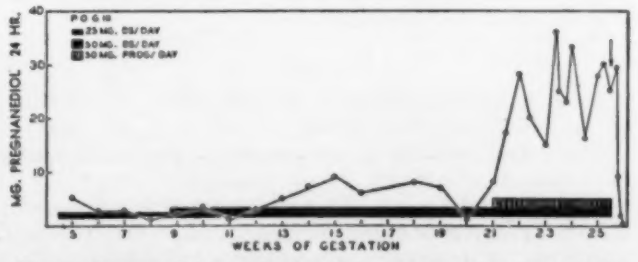


Fig. 7.—Pregnanediol excretion in third pregnancy of patient receiving diethylstilbestrol (25 mg. daily to ninth week and 50 mg. daily thereafter) and progesterone, 50 mg. daily, from the twentieth to twenty-sixth week. In this and succeeding illustrations PROG indicates progesterone.

Mrs. B. (fig. 9) had five pregnancies which terminated in abortion. In the sixth pregnancy she received 50 mg. of progesterone six times a week. This pregnancy terminated abruptly at about thirteen weeks. Although the conceptus had

undergone some degeneration, it was apparently normal. Pregnanediol levels were maintained above the average level because of the administered progesterone.

Mrs. C. (fig. 10) had one living baby which was delivered prematurely, following which, three consecutive pregnancies ended in abortion prior to twenty-six weeks. In the fifth

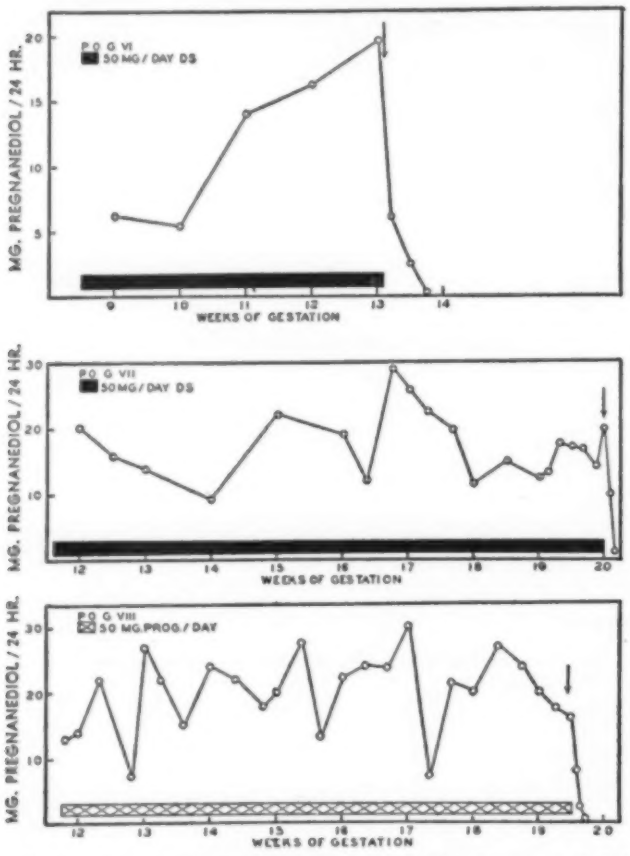

P O G VI
50 MG / DAY DS
MG. PREGNANEDIOL / 24 HR.
WEEKS OF GESTATION
P O G VII
50 MG / DAY DS
MG. PREGNANEDIOL / 24 HR.
WEEKS OF GESTATION
P O G VIII
50 MG PROG. / DAY
MG. PREGNANEDIOL / 24 HR.
WEEKS OF GESTATION

Fig. 8.—Pregnanediol excretion of patient receiving 50 mg. of diethylstilbestrol daily in sixth pregnancy (top portion) and in seventh pregnancy (middle portion) and 50 mg. progesterone in eighth pregnancy (bottom portion).

pregnancy (upper curve) she received 50 mg. of diethylstilbestrol daily. The curve of pregnanediol excretion was within normal limits. The syncytial phase of progesterone production showed a good response. The patient delivered a living previable fetus at twenty-six weeks, when free pregnanediol output was near its peak.

In her sixth pregnancy 50 mg. of progesterone was administered at almost daily intervals. This pregnancy was entirely uneventful, and she gave birth to a living baby at term. There were wide fluctuations in the pregnanediol curve (lower portion of fig. 10) but the general pattern was normal. It is impossible to assess the role of supplementary progesterone in this pregnancy.

COMMENT

In a small but carefully selected group of patients, an attempt has been made to evaluate the use of diethylstilbestrol and progesterone in the maintenance of pregnancies in which the prognosis for living children was exceedingly poor. It was not possible to uncover all the recurrent etiologic factors for the repeated abortions. However, all obvious physiologic and anatomic factors that might be implicated in the abortions and amenable to therapy were corrected. The primary objective of this study was to determine whether additional hormonal support was necessary for a successful pregnancy in these handicapped women and how best it could be provided. Furthermore, an attempt was made to determine whether this additional hormonal support could overcome some of the deleterious influences of recurrent factors responsible for the disastrous pregnancies.

If additional hormonal support is to be provided to improve the prognosis of women with habitual abortion, how is it to be provided? Is it most effective in the form of pure substitution therapy, or is it to take the form of administering substances that would stimulate the organism to provide adequate support of its own? Obviously, the latter approach is the more physiologic, for healthy endocrine function by the conceptus should be more conducive to a robust gestation than simple substitution. It should be recalled, however, that in endocrinology there is little evidence that inadequate glandular function can be stimulated by medication.

There is no evidence in this study that diethylstilbestrol stimulates steroid production by the corpus luteum or the syncytium. The Smith thesis, developed as a result of much painstaking work on the metabolism of estrogens, has been supported by the clinical observation that diethylstilbestrol administered to patients during pregnancy results in an increase in urinary pregnanediol. The withdrawal of this substance results in a drop of the titer. Thus, quantitative pregnanediol determinations presumably reflect the level of progesterone production by the corpus luteum and the placenta. However, we have not been able to confirm this observation.

In our search for an explanation for this discrepancy, we reviewed the metabolism of diethylstilbestrol. Mazur and Schorr in 1942 [19] injected this estrogen into rabbits and recovered 30 per cent as monoglucuronides from the urine. Smith and Williams in 1948 [20] confirmed this observation and found that a high percentage of the several synthetic estrogens examined are excreted in the urine as glucuronides. The Smiths have used the Venning method for the determination of pregnanediol, and this procedure measures the glucuronide titer in the urine. In the patient receiving diethylstilbestrol the result obtained by the Venning

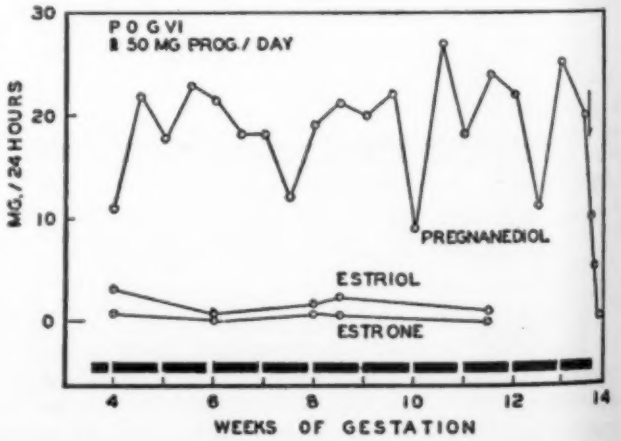


Fig. 9.—Pregnanediol excretion of patient in sixth pregnancy receiving 50 mg. of progesterone six times a week.

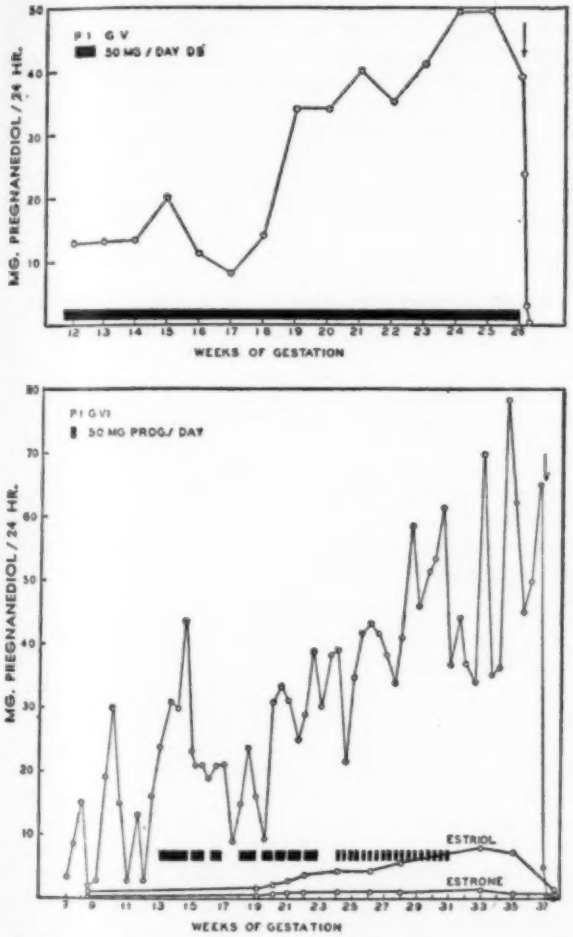
method would reflect the patient's progesterone metabolism as well as the glucuronides formed by the conjugation of the ingested diethylstilbestrol. We have recently confirmed these observations by simultaneous determinations of values for pregnanediol (Venning

19. Mazur, A., and Schorr, E.: Isolation of Stilbesterol Monoglycuronide from Urine of Rabbits, J. Biol. Chem. **144**: 283, 1942.

20. Smith, A. E. W., and Williams, P. C.: Urinary Elimination of Synthetic Oestrogens and Stilbestrol Glucuronide in Animals, Biochem. J. **42**: 253, 1948.

method) and a free pregnanediol in patients who were taking diethylstilbestrol and in pregnant women who were receiving no medication.[21]

If diethylstilbestrol, because of some action other than its estrogenic one, does not stimulate the corpus



10.—Pregnanediol excretion of patient receiving 50 mg. of diethylstilbestrol daily in fifth pregnancy (upper portion) and 50 mg. of progestetrone daily in sixth pregnancy (lower portion).

luteum and the syncytium to promote the production of increased amounts of steroids, does it have a place in the therapy of early and late pregnancy complications? This question cannot be answered until much more carefully accumulated data become available. It is a potent estrogen, and its estrogenic action may aid in early growth and vascularization, which are the bases of a healthy pregnancy. This tremendous growth-promoting force residing in estrogens may occasionally be useful in bolstering deficient hormonal support of a gestation.

It is more logical to substitute for inadequate progesterone production by administration of that substance. It is the pregnancy hormone and plays an important role in the successful establishment of the pregnancy. This and other studies indicate that its continued availability in increasing amounts is necessary for the successful maintenance of the pregnancy. Premature failures in hormonal support indicated in low pregnanediol titers spell disaster for the gestation. It is logical to substitute for an insufficient supply of this steroid by the administration of progesterone. Our previous experiences with such medication offer no substantial evidence as to its value, for small amounts only have been administered. Our evidence would indicate that less than one third of injected progesterone in a pregnant patient is reflected in pregnanediol excretion. If the patient excretes 40 or 50 mg. of pregnanediol each day at midpregnancy, it is likely that three or four times this amount of progesterone is available. Thus, to substitute adequately for an inadequate corpus luteum or syncytium would require 50 to 100 mg. of progesterone per day or even greater amounts. Until such adequate supplemental therapy is tried, the role of progesterone in the treatment of early pregnancy complications will not be known.

It must not be forgotten that, although adequate hormonal support is essential for a normal pregnancy, a normal conceptus and a favorable environment are equally important. It is possible that ideal hormonal support may overcome some deficiencies, but it will not make up for all of them. More knowledge concerning the physiologic factors of pregnancy and the intensive study of small groups of patients will eventually provide a pattern for therapy for early pregnancy complications. There is still no utopian hormone that will safeguard all pregnancies and assure living babies.

CONCLUSIONS

Two carefully selected groups of women with habitual abortion were studied in one or more pregnancies. Large doses of diethylstilbestrol were administered to one group and progesterone in oil to the other group. The course of each pregnancy was followed by periodic quantitative determinations of free pregnanediol, chorionic gonadotropins and estrogens. Living children were delivered to 45.2 per cent of the women treated with diethylstilbestrol and 66.7 per cent of the group treated with progesterone.

There is no evidence in this study that diethylstilbestrol stimulated the production of steroids by the corpus luteum and syncytium. Large amounts of progesterone may bolster failing hormonal support in the critical early period of a gestation. However, much more data is necessary to establish the value of such therapy. More intensive research in the physiologic norm of pregnancy will ultimately provide a rational regimen for the therapy of early pregnancy complications.

5841 Maryland Avenue.

ABSTRACT OF DISCUSSION

DR. O. WATKINS SMITH, Boston: There are now three reports on the treatment of chronic abortion with steroid hormones that have dealt exclusively with patients who had three or more consecutive abortions prior to the pregnancy studied: Dr. Davis's present paper; a report by Drs. Vaux and Rakoff on 24 patients who were given estrogen and progesterone with a 67 per cent fetal salvage, and the report of associates and I on 38 such women given diethylstilbestrol alone according to our dosage schedule with an 87 per cent fetal salvage. In all these reports clinical results were significantly better than would have been possible without treatment. Therefore, steroid hormones will save a large number of these pregnancies. The only question is, how should they be given for the best possible results? I would like to point out that there is no significant difference between Dr. Davis's results with progesterone alone and with diethylstilbestrol alone. It seems apparent that steroid hormones alone cannot help all these women; in some of them the primary cause may be a pathologic conceptus or a dietary, metabolic or even anatomic deficiency. We are grateful to Dr. Davis for his understanding of our basis for the use of diethyl-

21. Davis, M. E., and Fugo, N. W.: Does Administration of Diethylstilbestrol to Pregnant Women Result in Increased Output of Urinary Pregnanediol? Soc. Exper. Biol. & Med. **69**: 436, 1948.

stilbestrol not as a substitutional estrogen but as a stimulator for the endogenous production of estrogen and progesterone. We are greatly disappointed, however, that he failed to grasp the whole of our concept and the importance of grading the estrogen dosage according to the physiologic levels of normal pregnancy. His dosage starts at a level far in excess of what we would consider physiologic and does not even faintly resemble our carefully worked out schedule as pregnancy progresses. Our experimental observations, as well as clinical experience, have indicated that the dosage is important in maintaining the stimulative effect on steroid secretion. We are not surprised that his results, although good, are significantly less good than ours. Drs. Davis and Fugo found that when pregnanediol is measured by the Venning method, which recovers and weighs pregnanediol glucuronide, a definite rise follows therapy, with a drop when medication is discontinued. They have made the important observation, however, that diethylstilbestrol causes no increase in pregnanediol excretion when this metabolite of progesterone is measured on hydrolyzed urine by the sulfuric acid color reaction. This second observation has been confirmed by Professor Marrian of Edinburgh, Scotland, and by us. For the past year we have been attempting to find the explanation of this discrepancy. The possibility that diethylstilbestrol glucuronide was being recovered by the Venning procedure in more than trace amounts was considered by us some years ago and rapidly eliminated. The more likely explanation, and one for which there was some indication long before we started our recent studies, is that the discrepancy in results between the two methods can be attributed to the recovery, by the Venning procedure, of pregnan 3 (α)ol-20-one glucuronide.

Dr. A. E. Rakoff, Philadelphia: Comparative studies in women with true habitual abortion by a single group of investigators provides the best type of clinical experiment for the statistical evaluation of substances which might prevent the recurring factor causing abortion in so high a percentage of the next pregnancies. To correct patients who have had the prerequisite of three consecutive abortions, to rule out all but the genetic and endocrine factors and then to persist with a treatment by plan in these women who so desperately desire a child is no easy task, but it adds much significance to the value of this excellent study. If sufficient patients were available, one could suggest several other groups to complete the comparative evaluation of the supportive measures and general advice given to these patients, for instance, one group receiving large amounts of chorionic gonadotropin, another receiving a combination of estrogen and progesterone, and a control group receiving no steroid therapy. I should be the last to suggest this control group, since I have not had the temerity to employ it in my own study in these women who so ardently desire to have babies. I have been particularly impressed by the rationale of combined estrogen and progesterone therapy, since both these steroid hormones appear to be made by the same cells in the corpus luteum and in the placenta, and their curves parallel each other as pregnancy progresses. Furthermore, low pregnanediol values are regularly accompanied with low serum estrogen titers in my experience. Also, titers of chorionic gonadotropin in these patients were usually within normal range, and even if substitutional therapy would seem to offer a more certain means of providing the estrogen and the progesterone rather than stimulation therapy with chorionic gonadotropin. Drs. Davis and Fugo found in this study that high dosage progesterone therapy afforded equal or better prophylactic results than did large doses of diethylstilbestrol. This is a point which deserves to be stressed, in view of the growing use of high dosage diethylstilbestrol treatment. Even the salvage rate of 45.2 per cent in the diethylstilbestrol-treated group is considerably better than the less than 16 per cent which one would expect from statistical evidence based on the poor performance of these women in earlier pregnancies.

Dr. A. B. Abarbanel, Los Angeles: Results of associates and me with diethylstilbestrol were the same as the results of Drs. Davis and Fugo with progesterone. There is more than one factor involved. In a recent study, in the group of women who abort between the twenty-second and seventieth days of pregnancy, we found that the control group treated with placebos gave a 20 per cent salvage, whereas the group treated with diethylstilbestrol gave a 37 per cent salvage; the salvage is so poor in this group primarily because most of these women are poor pregnancy risks to start with. Between seventy and one hundred days, that is, ten and fourteen weeks of pregnancy, the control group treated with a placebo showed 54 per cent salvage against a 78 per cent salvage in women treated with diethylstilbestrol. The mechanism by which diethylstilbestrol may salvage these pregnancies is primarily the maintenance of the vascular bed—in other words, the soil in which the roots of the fetus are growing. If the vascular bed is good, the struggle for existence of this particular egg will be successful. Some women will stop bleeding and having cramps with dosages as low as 1 mg. of diethylstilbestrol a day, and others may require 500 mg. It is most important to give that amount which will stop the bleeding. We have found that dosages as high as 10,000 mg. a day will not cause abortion. In 1938 Parks reported that he was able to cause abortion in a cow by means of diethylstilbestrol. Accordingly, we tried to cause abortion in human beings, when a therapeutic abortion was indicated, by means of diethylstilbestrol alone, and in 1941 we reported that we were unsuccessful. Dr. Karnaky of Texas went one step further and found that he could stop the bleeding and cramps of threatened abortion in early pregnancy, and so reported his results in 1942. We are indebted to him primarily and to the laboratory work of the Smiths for this particular era, in which steroid therapy, be it estrogen or progesterone, or both, has evolved to the point where we are now able to salvage a much larger number of threatened pregnancies.

Dr. Karl John Karnaky, Texas: Eleven years ago we began to experiment with diethylstilbestrol in Houston, Texas, and observed that the agent was of value in abortions and in uterine bleeding. We gave it to patients with uterine bleeding associated with pregnancy, and in most patients cramping and bleeding ceased; a large percentage delivered normal babies at term. Thus we discovered that diethylstilbestrol was of value in threatened and habitual abortion, premature labor and some other accidents of pregnancy. Prior to 1941 it had been taught that estrogens caused abortions and were contraindicated in pregnancy. It was hard to convince the members of the medical profession that estrogens were of value in such cases, but with the aid of Drs. Abarbanel, Rosenblum, Smith of Boston and others, the newer concept has been accepted. Diethylstilbestrol has been proved a harmless drug in our studies. The dose required to prevent accidents of pregnancy varies with each patient. If there are no signs or symptoms of abortion at this pregnancy, and as soon as the basal temperature remains above 98 F. for seven days, one-fourth of a 25 mg. (6.25 mg.) micronized diethylstilbestrol tablet is given nightly; every fourth night the dose is increased by one-fourth of a 25 mg. tablet until one 25 mg. tablet is being taken nightly. If any signs or symptoms of abortion begin, four 25 mg. tablets are taken every fifteen minutes until all signs and symptoms are controlled. It usually takes two to six doses. Then 50 mg. are taken nightly for seven nights. Then the dose is dropped back to 25 mg. nightly. For years I have tried to work out a dose schedule for these cases, but the dose was found to be so variable that I gave up the idea. It is impossible to give too much diethylstilbestrol, but too little is possible. The larger the daily dose of diethylstilbestrol, the more certain it is that the patient will carry her pregnancy to term and deliver a normal child. In several hundred cases of threatened and habitual abortion and premature labor we have found progesterone useless. We have found only diethylstilbestrol necessary.

Dr. M. Edward Davis, Chicago: Dr. Fugo and I have been disturbed for a long time by the fact that we could not obtain the results reported by the Smiths. Apparently the discrepancy arose because in our laboratory free pregnanediol was determined, whereas the Venning method used by the

Smiths is a measure of the total glucuronide titer of the urine. It is of great interest to hear that Dr. Olive Smith is continuing her work on other metabolic products of progesterone metabolism. The group of patients is too small for positive conclusions as to the results of therapy. It is interesting that the use of large amounts of progesterone was followed by a greater salvage of pregnancies than the administration of diethylstilbestrol. It seems much more logical to substitute adequately for progesterone deficiency by administering this hormone than to depend on diethylstilbestrol to stimulate the placenta to produce more steroids. We have no good evidence that this can be done. The amount of progesterone necessary to maintain a pregnancy is not known, but our work would indicate that at least 50 to 100 mg., parenterally given, is necessary each day. Perhaps such additional hormonal support will help to maintain a pregnancy which would have terminated disastrously.

STATUS ASTHMATICUS

GEORGE PINESS, M.D.
Los Angeles

In 1933 Clarke[1] described status asthmaticus as a period of intense dyspnea which lasted a few days to a week (occasionally longer) and was caused by an outpouring of viscid mucus into the bronchioles, resulting in a serious loss of lung capacity and a corresponding failure to respond to the ordinary dose of epinephrine. Death more commonly results in this than in either of the other commoner types of asthma, acute bronchial asthma and chronic or intractable asthma. The last may be defined as a persistent and refractory type that is unyielding to presently available therapeutic measures. The patient is seldom free of symptoms, and the disease is usually associated with chronic bronchitis, bronchiectasis and emphysema. When an acute asthmatic attack fails to subside and becomes refractory to the usual palliative measures which in the past gave relief, the dyspnea becomes severer, cough is unproductive and epinephrine hydrochloride therapy is ineffective despite larger doses and more frequent administration; the patient appears critically ill and remains in a constant asthmatic state.

Clinical Description.—Clinically the patient presents a picture of extreme, constant dyspnea of a wheezy nature. He assumes the upright posture to effectively employ the voluntary muscles of respiration. He has an unproductive cough and cold clammy skin, and he may be cyanotic. The temperature may be elevated. The pulse rate is rapid and may be irregular. The patient appears frightened and fatigued; his entire being is so concentrated on the exhausting demand to breathe that it is difficult to obtain his cooperation. Unconsciousness or disorientation may occur suddenly; a loose cough will develop and produce large amounts of mucus, and the dyspnea will subside. The elevation of temperature in the presence of pulmonary signs may appear to be that indicative of pneumonia. Such signs as consolidation and leukocytosis are characteristic of bronchial obstruction. These patients usually make an uneventful recovery. The duration of the obstruction varies from a few days to a week and occasionally longer. Death occurs more often in status asthmaticus than in uncomplicated acute or chronic asthma.

Physical Signs.—At the onset one hears dry, sibilant and sonorous rales scattered throughout the chest. Breathing is wheezy, and occasional moist rales are heard in various areas, changing from one area to another of the lung. Breath sounds may be loud and clear in one area and distant in another. Expiration is prolonged, and expansion may be diminished. If pneumonia occurs, there will be bronchial breathing and dulness on percussion. Usually this phase is of short duration with complete recovery.

Etiologic Basis.—I am of the opinion that status asthmaticus is frequently the result of conditions imposed on and by the patient who has acute asthma. Observations made on a large number of patients in status asthmaticus indicated that they usually were overmedicated, lacked sufficient fluids and food, and oftentimes employed medicaments that checked cough and production of secretions.

THERAPEUTIC MEASURES

Therapy should be directed first toward assuring the patient that the attack is controllable and that his cooperation is necessary to obtain results. The patient should be hospitalized in a private room to assure rest. The room should be as bare as possible, and all pillows and mattresses should be nonallergenic or in plastic casings. Symptomatic treatment should be particularly directed toward keeping the air passages open and liquefying bronchial secretions. Since the patient in status asthmaticus fails to respond to ordinary doses of epinephrine given subcutaneously and even to larger doses given at frequent intervals, these patients appear to be epinephrine-fast. One may give epinephrine intravenously in a 0.1 cc. dose diluted in a small amount of isotonic sodium chloride solution. If this fails to relieve the patient, epinephrine administration should be discontinued entirely.

In the prolonged attacks of status asthmaticus the patient has had little nourishment and an inadequate amount of fluids, resulting in hemoconcentration and acidosis. To combat the foregoing factors, intravenous administration by the drip method of 5 per cent dextrose in distilled water should be maintained continuously or repeated at three to six hour intervals until such time as they are satisfactorily controlled. The average patient will require 3 to 5 liters of fluid by the intravenous route in twenty-four hours.

Iodine is the best drug available for liquefying bronchial secretions. It may be given orally as a saturated solution of potassium iodide in 20 to 30 minim (1.23 to 1.85 cc.) dosage three times daily or intravenously as sodium iodide; 1 Gm. may be added to a liter of the solution for intravenous administration by the drip method if the patient is unable to take the drug orally.

Aminophylline (theophylline ethylenediamine) has received widespread acceptance as a bronchodilator in the treatment of bronchial asthma. It has been recommended by Unger and Goodall[2] in treatment of status asthmaticus. They suggested that the patient receive 3.75 Gm. of the drug intravenously on admission to the hospital, then be given 0.5 Gm. intravenously dissolved in 1,000 cc. of 5 per cent dextrose over a period of three or four hours. This liter infusion is repeated daily for three or four days if necessary. They expressed their belief that this procedure keeps the bronchial musculature relaxed by the continuous

Read before the Section on Miscellaneous Topics at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. Clarke, J. A.: J. Allergy **4**: 481-484, 1933.

2. Unger, L., and Goodall, R. J.: Ann. Allergy **5**: 196-202, 1947.

infusion of the aminophylline. They reported brilliant results in 4 cases and failure in only 1.

Aminophylline in suppository form is available, but in my experience it has not proved beneficial: my use of this drug in status asthmaticus has not given satisfactory results regardless of the method. Fatal reactions have been reported by Bresnick and others.[3] Administration of oxygen and helium in combination or alone is indicated only in the presence of cyanosis. Barach has recommended a mixture of 80 per cent helium and 20 per cent oxygen.

Maytum [4] and Kahn [5] have recommended ether and oil in equal proportions given rectally. Maytum suggested use of 1 ounce (28 Gm.) of mixture to 20 pounds (9.1 Kg.) of weight. Kahn suggested that twenty minutes be taken in administering the mixture, using a glass syringe and rubber tubing and depending on gravity to carry the mixture to the bowel.

Caffeine alkaloid orally, 3 grains (0.19 Gm.) every three to four hours, or caffeine and sodium benzoate 7½ grains (0.5 Gm.) given subcutaneously every three hours is effective when the patient is epinephrine-fast. It does stimulate the patient and has bronchodilator ability. Morphine or comparable drugs as dihydromorphinone (dilaudid®) or meperidine (demerol®) are definitely contraindicated for use in status asthmaticus because they depress the cough reflex and the respiratory center and have a peripheral constricting action on the bronchial musculature. This is not in accord with the opinions of Clarke, Tuft [6] and Kahn,[7] who have stated their belief that small doses of morphine are necessary and desirable for sedation and mental relief.

For physical and mental sedation of the patient I suggest use of chloral hydrate, 2 Gm. alone or in combination with sodium bromide, or 4 Gm. diluted in 60 cc. of warm water given as a retention enema, or 0.5 to 1 cc. of chlorobutanol given orally. This does not cause respiratory depression, and sedation is excellent.

Alcohol in saline solution as recommended by Brown [8] did not give the satisfactory results he claimed for this therapy. There was no dramatic or quick relief for my patients.

Barbiturates in small doses, ¼ to ½ grain (15 to 30 mg.), at four hour intervals for mild sedation is recommended.

Bronchoscopy has been suggested as a means of removing mucous plugs and thick tenacious mucus from the bronchi. Excellent results have been reported by Waldbott [9] and others. My experience with this procedure is limited, since I have never found it necessary to employ this method.

OUTLINE OF THERAPY

The following plan of treatment has been found most satisfactory in caring for and giving relief to patients in status asthmaticus.

1. Hospitalization in a dust-free room if possible.

2. Force fluids:

(*a*) By mouth; water, fruit juices and carbonated drinks.

(*b*) By intravenous route; dextrose 5 per cent in distilled water or dextrose 5 per cent in saline solution, 3 to 5 liters daily until the patient is hydrated.

3. Sedation: Small doses of barbiturates, chloral hydrate or chlorobutanol.

4. Expectorant: Sodium iodide 1 Gm. intravenously or saturated solution of potassium iodide, 1 to 2 cc. three times a day after meals.

5. Bronchodilators: Aminophylline 7½ grains (0.5 Gm.) intravenously. Epinephrine 0.5 cc. as circumstances may require when patient is reactive to same. Caffeine alkaloid 3 grains (0.19 Gm.) every four hours or caffiene and sodium benzoate 7½ grains (0.5 Gm.) every four hours subcutaneously.

6. Oxygen or mixture of oxygen and helium when cyanosis is present.

7. Avoid at all times use of morphine, dihydromorphinone, meperidine and atropine in the patient with status asthmaticus.

SUMMARY

Intractable bronchial asthma and status asthmaticus are defined.

A brief description of the course, and symptoms of status asthmaticus is given.

Various therapeutic measures are suggested, and the literature is discussed.

A plan of treatment for relief of status asthmaticus is given in detail.

672 South Westlake Avenue (5).

3. Bresnick, E.; Woodard, W. K., and Sageman, C. B.: J. A. M. A. **136**: 397-398 (Feb. 7) 1948.
4. Maytum, C. K.: M. Clin. North America **15**: 201, 1931.
5. Kahn, I. S.: J. Allergy **10**: 262, 1937.
6. Tuft, L.: Clinical Allergy, Philadelphia, W. B. Saunders Company, 1937, p. 332.
7. Kahn, I. S.: Tri-State M. J. **14**: 2785, 1942.
8. Brown, E. A.: Ann. Allergy **5**: 193, 1947.
9. Waldbott, G.: Paper read at the meeting of the Academy of Allergy, December 1948; unpublished data.

ABSTRACT OF DISCUSSION

Dr. Maurice S. Segal, Boston: It seems that along the Atlantic coast line one sees a much more serious type of status asthmaticus with a wide variety of complications, particularly sinobronchitic disease, pulmonary fibrosis and pulmonocardiac failure. One has to resort to more intensive procedures to cope with the problem. Administration of epinephrine and all synthetic derivatives by all routes should definitely be stopped in status asthmaticus. I have found helpful a continuous intravenous infusion of aminophylline. The technic should be modified according to the individual. Generally, it is of benefit to give 3 liters of fluid in twenty-four hours, at a rate of flow of about 30 drops per minute. The first liter may be 5 per cent dextrose in isotonic sodium chloride solution and the second and third liters 5 per cent dextrose in distilled water. Aminophylline, up to 0.5 Gm. per liter of solution, is added. These infusions may be continued for several days and in many cases have been continued as long as two weeks. This therapy may be interrupted, depending on the patient's condition. I have found it helpful to introduce an antihistaminic agent at four to six hour intervals directly into the tubing, close to the needle. This is of particular value in restoring the histamine-sympathin balance in the epinephrine-refractory state. On occasion meperidine hydrochloride (demerol hydrochloride®) may be given in similar fashion. Bronchoscopy should be resorted to much more commonly than it has been. I generally advise vinyl ether (vinethene®) induction of anesthesia, followed by general ether anesthesia (preferably the closed circuit method), supplemented with an ample flow of oxygen or helium and oxygen if available. I have found topical anesthesia, particularly with tetracaine (pontocaine®) and to a lesser degree with cocaine, dangerous in these patients. Bronchoscopic aspiration should be thorough and may be repeated if indicated. Irrigation of the bronchi with isotonic sodium chloride solution and instillation of antibiotic agents may be performed if there is evidence of considerable bronchitic infection. Administration of oxygen is indicated in the cyanosed patient. Helium and oxygen mixtures under positive pressure are preferable when it is evident

that there is considerable obstruction. The concentration of helium should not be below 60 per cent. Unfortunately, use of the hood apparatus whereby one can obtain positive pressure in both inspiration and expiration requires skilled technical assistance. One should avoid confusional therapy and substitute sound physiologically directed therapy in the management of this serious disease.

DR. MEYER A. RABINOWITZ, Brooklyn: When one sees a moribund patient with asthma, one does not have much time to do many of the things that have been outlined. One must make a rapid decision. Is the patient dying of right-sided heart failure or is he dying of suffocation? About a month ago I was called to see a patient who was getting oxygen, aminophylline and digitalis, with a diagnosis of right-sided heart failure. The patient was cyanotic and unconscious, not just stuporous. At once it was realized that the absence of distended veins of the neck, or enlargement of the liver, the patient was not suffering from right-sided heart failure. Fortunately, the patient was in the hospital. I sent at once for an anesthetist, who intubated the patient and aspirated considerable inspissated material. The next day the patient was perfectly comfortable and had absolutely no recollection of my ever having been there.

DR. BRET RATNER, New York: One of the prime situations in status asthmaticus, particularly in children, is the existence of an obstructive state, such as inspissated mucus. Years ago I suggested that perhaps the best method of removing inspissated mucus was by forceful emesis. I have introduced the use of ipecac for this condition, and there are physiologic reasons for assuming that a reverse peristalsis is set up in the lower bronchial tree, which brings this plugged mucus out from above the corina. Then the patient can expel the one major cause of status asthmaticus. Bronchoscopy is a serious procedure, particularly in children. I would urge every one to try giving, in severe status asthmaticus, an emetic dose of ipecac, and you will be rewarded at times by witnessing a brilliant remission of this dreadful condition. I have had one instance of a child, 13 years of age, who had complete atelectasis of the lower lobe of the right lung, shown by roentgen examination. I gave this child 2 teaspoons (7.4 cc.) of syrup of ipecac. The child had forceful vomiting and within a short time was cleared of the condition, which was originally diagnosed as empyema. The following day another roentgenogram was taken, which showed a complete absence of any pathologic condition.

DR. GEORGE PINESS, Los Angeles: Dr. Ratner is not original in his idea about ipecac. It was advocated many years ago in the old pediatric and medical textbooks. Its use as suggested by him is a well worth while addition to our armamentarium of therapy. But when the child is in status asthmaticus it is usually because he has stopped eating and drinking. Making him vomit won't bring up a thick inspissated plug of mucus in the bronchus; fluids will. Dr. Segal mentioned that the physician must not become confused, apprehensive and panicky, since a patient with status asthmaticus seldom dies unless he is treated as the patient mentioned by Dr. Rabinowitz. It would be unlikely that a patient of mine in any hospital that I was connected with would ever get to that stage unless an intern or someone else inadvertently gave him an injection of morphine or some other opiate. One should get the confidence of the patient with status asthmaticus and also assure him that he is not going to die. I think that is important. I have not found an occasion to use bronchoscopy to save anybody's life to date. I also want to mention that bronchoscopy is a major procedure when a patient is as sick as the person with status asthmaticus. I agree with Dr. Rabinowitz that bronchoscopy was indicated in his particular case. That was a case in which someone had been negligent, and I am sure that the patient and everyone concerned appreciated the prompt, excellent care that Dr. Rabinowitz gave in that instance. The problem of therapy for these patients is simple, and the results are as good as the patience shown by the attending physician. If he knows what he is doing, he will have no trouble in getting a patient over the condition. I do not think that there are any more cases of status asthmaticus or that they are any more severe in Boston than they are in Los Angeles.

URINARY TRACT CALCULI IN RECUMBENT PATIENTS

COL. JAMES C. KIMBROUGH, M.C.
MAJOR JOSEPH C. DENSLOW, M.C.
and
MAJOR DAVID K. WORGAN, M.C.
Washington, D. C.

The management of 15 recumbent patients with bone injury (not including paraplegic patients) who formed urinary calculi, observed during the year May 1, 1947 to May 1, 1948, was reported last year before the American Urological Society.[1] Approximately 800 recumbent patients with bone injury were hospitalized at Walter Reed General Hospital in that period. The incidence of the low percentage (2 per cent) of calculus formation in such a large number of patients with similar injuries, hospitalized under almost identical management, makes it evident that there is a stone diathesis due to general derangement of calcium metabolism and/or local factors in the urinary tract.

The shortest period required for the formation of stone was 74 days, the longest 1,200 and the average 362. When we disregard the longest and shortest cases, the mean time was 272 days.

The following preventive regimen was carried out so far as possible:

a. Maintain fluid intake at a minimum of 4,000 cc. daily.

b. Avoid stasis: move the patient; change his position every two hours when feasible. Give attention to anomalies favoring stasis, ureteral obstruction, hydronephrosis and congenital anomalies.

c. Remove focal infection: give proper treatment of osteomyelitis.

d. Eradicate urinary tract infection: employ chemotherapy; correct stasis.

e. Employ dietary measures: prescribe acid ash diet; high vitamin A and B; limited calcium intake.

f. Give aluminum hydroxide gel and estrogens to increase urine acidity and to decrease phosphorus and calcium output and precipitation.

g. Give medication to acidify urine—sodium biphosphate or mandelic acid.

h. Follow patient adequately; culture urine frequently; make roentgen examination of urinary tract every three months; make excretory urograms as necessary.

The magnitude of the almost impossible task of enforcing such a plan for 800 patients can be appreciated. Since less than 2 per cent formed calculi, an effort was made to ascertain the patients susceptible to this formation before the calculi appeared. This information enabled the ward physician to concentrate on a rigid regimen for those who were probable stone formers and use general measures for the 98 per cent who were not susceptible.

METHOD OF STUDY

The work of giving special examinations to all the 800 patients proved to be almost impossible, so that the selection of patients for the rigid regimen became necessary. On admission the patients whose recumbent expectancy was more than three months were divided into the following classes and subclasses:

1. Patients with a negative history of urinary tract disease.

Read before the Section on Urology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

From the Surgical Service of Walter Reed General Hospital: Chief, Section of Urology (Colonel Kimbrough); Senior Resident in Urology (Major Denslow), and Assistant Chief, Urology Section (Major Worgan).

1. Kimbrough, J. C.; Denslow, J. C., and Worgon, D. K.: Urinary Tract Calculi in Recumbent Patients, J. Urol. **61**: 5 (May) 1949.

2. Patients with a positive history of urinary tract disease: calculi, infection, stasis and/or severe prolonged focal infection, such as intractable osteomyelitis.

The patients in class 2 who required long recumbency were given the following examinations as soon as their condition would warrant: (1) urine culture; (2) serum calcium and serum phosphorus determination; (3) urinary calcium, twenty-four hour excretion on regular diet and low calcium and acid ash diet; (4) excretory urogram; (5) cystoscopy and retrograde urogram when indicated, and (6) evaluation of focal infection and osteomyelitis.

This made it possible to divide the recumbent (class 2) patients susceptible to calculi formation into three subclasses:

Subclass 1. Those with normal urinary tract, normal calcium metabolism and without focal infection.

Subclass 2. Those with minor changes in the urinary tract and/or calcium metabolism.

Subclass 3. Those with pronounced changes in the urinary tract and/or calcium metabolism.

Patients in class 1 and subclass 1 (class 2) were given general care, regular diet and high fluid intake. Those in class 2, subclass 2, were given a moderate regimen of diet and fluid intake. Patients in class 2, subclass 3, were given the rigid calculi-preventive treatment previously outlined. Urinary tract infection was given adequate treatment, and focal infection was eliminated in all cases.

Except in gross disease of the urinary tract and parathyroid disease the volume of urinary output (fluid intake) is the most important factor in preventing the formation of stones.

Freeman [1a] stated that calculi will not form if the calcium output is kept below 15 mg. per hundred cubic centimeters. A urine output of 3,000 cc. daily will prevent calculi in a 450 mg. daily calcium output. With rigid regimen it is possible to maintain these two conditions (3,000 cc. urine output and less than 450 mg. calcium output) in almost all cases.

Sodium biphosphate, as emphasized by Cordonnier and Talbot,[2] possesses special properties for reducing the amount of total calcium excretion.

WATER SUPPLY

A comparative study of the hardness of the water supply for representative cities in the United States was made. The total hardness of the water supply to Washington, D. C., and Walter Reed General Hospital is 105. The hardness of the city supply in general for the United States ranges from 53 to 130. This uniform hardness is maintained by softening processes and other measures. It is evident that the hardness of the water supply is not a factor in the incidence of urinary calculi in the patients in Army hospitals in the United States.

MATERIAL

Other than paraplegic persons, 864 recumbent patients with bone injury were hospitalized on the Orthopedic Section of Walter Reed General Hospital during the last year, May 1, 1948 to May 1, 1949. Patients who required three months of bed rest were classed as recumbent. All these patients were not confined to bed the entire time. Many had multiple operations and were ambulant between operations. During this year only 2 patients were observed with urinary calculi; the calculi had already formed in 1 patient when he was transferred from another hospital, and the other patient was admitted Feb. 18, 1948 because of multiple fractures of extremities and head injuries. He was comatose three months, during which time adequate stone-preventing care could not be properly maintained. This compares favorably with the incidence of 15 cases of urinary calculi reported last year (May 1, 1947 to May 1, 1948) and is evidence of the efficiency of the present regimen.

In order to establish a basis for comparison in selecting patients for preventive treatment the following calcium studied were conducted:

1. A series of 10 ambulatory patients without a history of calculi had daily urinary calcium estimation. The lowest value was 142 mg., the highest 445 mg., the average 265 mg., per hundred cubic centimeters. All had normal serum calcium and serum phosphorus levels.

2. A series of 10 ambulatory patients with urinary tract calculi was given similar examination on regular diet and on acid ash, low calcium diet. The average daily urinary calcium excretion on regular diet was 259 mg. per hundred cubic centimeters, on an acid ash low diet in calcium 176 mg.—a reduction of 32 per cent. The serum calcium and phosphorus levels were normal in all patients.

3. Ten consecutive recumbent patients with a negative history of urinary tract calculi had an average daily urinary calcium excretion of 291 mg. per hundred cubic centimeters on an acid ash diet low in calcium. These patients had been recumbent four to twelve months.

It is apparent that daily urinary calcium excretions above 225 mg. per hundred cubic centimeters should require special evaluation. The series of 15 recumbent patients with calculi reported last year all had daily urinary calcium excretion above 250 mg.

The history of the 2 patients who formed calculi this year is as follows:

REPORT OF CASES

Case 1.—A man aged 18 was admitted to Walter Reed General Hospital by transfer Feb. 18, 1948. The diagnoses were simple complete fracture of the upper third of the left femur and compound comminuted fracture of the right tibia and fibula, middle third; abrased lacerated contusion of face and scalp; encephalopathy, chronic, due to undetermined cause; calculus in pelvis, right kidney; decubitus ulcer of the skin over the sacrum, and calcified subperiosteal hematoma of the right and left humerus. He was immobilized one hundred and seventy-eight days by bed rest and traction. A staghorn calculus in the right kidney was diagnosed by roentgen ray Sept. 14, 1948. Treatment of the calculus by right pelviolithotomy was performed Nov. 18, 1948. Urine culture revealed Streptococcus fecalis. The serum calcium determination was 11.8 mg. and the serum phosphorous 3.1 mg., per hundred cubic centimeters. Urinary calcium output values on two occasions were (1) 45.39 mg. and (2) 64.0 mg. per twenty-four hours. The low urinary calcium output was verified. No explanation for this low output could be ascertained. This patient was comatose more than three months following his injury, and adequate preventive calculus treatment could not be given.

Case 2.—A man aged 22 was admitted to Walter Reed General Hospital Sept. 29, 1948. He had been injured by gunshot wound in the left femur, tibia and fibula April 8, 1945. He was immobilized 1,095 days in Thomas splint and traction. Ureteral calculus with stricture was diagnosed by roentgen ray April 26, 1946. Treatment of the calculus by nephrolithotomy and intubated ureterotomy was performed March 18, 1949. A contribu-

1a. Freeman, L. W.: Metabolism of Calcium in Patients with Spinal Cord Injuries, Ann. Surg. **129**: 177 (Feb.) 1949.

2. Cordonnier, J. G., and Talbot, B. S.: Effect of the Ingestion of Sodium Acid Phosphate on Urinary Calcium in Recumbency, J. Urol. **60**: 316 (Aug.) 1948.

tory pathologic condition was stricture of the upper third of the ureter. The serum calcium level was 10.8 mg., the serum phosphorus 4.1 mg., per hundred cubic centimeters, and the urinary calcium output 260 mg. per twenty-four hours. Calculus was present in this patient on transfer to this hospital.

COMMENT

Two recumbent patients with bone injury formed urinary tract calculi at Walter Reed General Hospital during the year May 1, 1948 to May 1, 1949. During this period 864 recumbent patients were admitted. Special conditions were present in these two patients—in 1 the calculi had formed prior to admission; the other patient was comatose three months following injury. Parathyroid disease was not present. The present management has reduced the effort of general care, dietary regulation and other stone prevention measures to a minimum of work. Early ambulation and ambulation between the multiple operative procedures has been a major factor in maintaining the low incidence of calculi.

CONCLUSION

With the proper selection few recumbent patients will require a rigid regimen to prevent urinary calculi. The calculi can be prevented in the majority of patients by maintaining adequate fluid intake and early if only partial ambulation.

A few selected patients will require a rigid regimen to prevent the formation of calculi. This selection of cases saves enormous effort in the care of the recumbent patient with bone injury.

ABSTRACT OF DISCUSSION

DR. RUBIN FLOCKS, University Hospitals, Iowa City: Colonel Kimbrough has had a marvelous opportunity to see and take care of recumbent patients. He is to be congratulated on his painstaking study of this particular problem. I also agree that it is perfectly possible, and it is the thing to do, to divide these patients into those who are susceptible, might form stones, and those who are not, and to treat intensively those who are susceptible. His method is good. He did not mention the estimation of serum protein in the study of his patients to rule out hyperparathyroidism, but he probably does that. Hyperexcretion of calcium in the patient who is recumbent is of importance from the standpoint of formation of the urinary stone only in the early period. After the patient has been immobilized for a month or six weeks, the urinary calcium level comes down and is within normal limits. In other words, the bony tissues get into equilibrium, and the urinary calcium is back to normal and no longer is likely to be a factor in stone formation. As soon as the patient has passed the initial six week period, even though he still is recumbent, without stone formation, the chances are he will not get one, as far as the urinary calcium is concerned, and that factor need no longer be taken into consideration.

DR. JOHN F. MCCUSKEY, Clarksburg, W. Va.: Drs. Kimbrough and Denslow are to be congratulated on their attack of this problem of calculi in recumbency from a biochemical point of view. It is apparent that recumbency is not the entire answer. During the war I ran a series of blood calcium determinations on ambulatory fracture patients and found that even in these cases during the first five days on controlled calcium intake the average blood calcium level was 13.8 mg. per hundred cubic centimeters. This is an appreciable increase even in ambulatory patients and was reflected in an increase of the urine calcium as determined by the Sulkowitch test. We found little or no change in blood phosphorus levels. As for treatment, mobilization of the patient and of body fluids are important. We were fortunate in our city to have one of the pioneers in metal fixation splint work. The Haynes splint, now in use, mobilized even the worst fractures. The Stader and Roger Anderson splints performed the same duty. Calculi in recumbency are less frequent in our locality. Ammonium chloride has a tendency to mobilize more calcium, and in addition if urea-splitting organisms are present the purpose is defeated. Use of sodium biphosphate was objectionable because it increased the phosphaturia. But we use it almost entirely now, having borrowed a trick from the internists. Aluminum hydroxide gel and similar substances will, when given simultaneously, combine with phosphates in the intestinal tract and leave an acid urine.

DR. HENRY SANGREE, Philadelphia: Dr. Kimbrough has shown in his large series of 864 cases that only 2 per cent of patients with bone injury formed urinary calculi. This agrees with the experience of associates and me, as we also found only a 2 per cent incidence in our small series. Dr. Kimbrough found no parathyroid disease in his large series. In our 50 cases we had only 1 patient with parathyroid disease who formed a kidney stone, and this was a case of tumor of the parathyroid. We commend early ambulation for these patients. We consider that the chemical method used in many hospitals for the diagnosis of urinary calculi is not accurate enough to diagnose the crystalline structure of urinary calculi. Certain calculi of the urinary tract can be prevented. Cysturia can be prevented with a proper dietary regimen. Uric acid calculi formed in patients with high blood uric acid can be improved by a proper medical and dietary regimen.

DR. JAMES C. KIMBROUGH, Washington, D. C.: I am deeply grateful to Dr. Flocks, Dr. McCuskey and Dr. Sangree for their complimentary discussion of this paper. There are many things in it that, in presenting it, might seem superficial but are really not in the original paper. In reply to Dr. Flocks, we have not found a variation in serum calcium and serum phosphorus, indicating parathyroid disease, in any of these fracture cases. There is high calcium excretion during early immobilization. However, our patients are usually hospitalized in a small hospital first. By the time we see them, they have been treated several weeks and the period of high calcium excretion has passed. We no longer use ammonium chloride, because it has been known for several years that it does favor the mobilization of calcium, a process in bone injury which is not too clear but is fairly well established. These ambulatory fracture patients were not walking on the fractured leg, and it was practically that much bone that was immobilized, in spite of the fact that the body was moving about. I am not sure how much difference there would be in the calcium mobilization in a bone injury case and in a case of immobilization from other disease, such as acute infection.

The Circle of Willis.—In man the brain is supplied with blood entirely by means of the paired internal carotid and vertebral arteries. There are no significant anastomoses with the extracerebral arteries such as exist in lower mammals. In general the internal carotid arteries supply the anterior and middle portions of the brain on each side while the single basilar artery formed by the union of the two vertebrals supplies the occipital lobes, portions of the temporal lobes and the structures in the posterior fossa. These three main sources communicate with each other at the base of the brain in the so-called circle of Willis, the two carotids by means of the anterior communicating artery and each carotid with the basilar by way of the posterior communicating arteries. Under normal circumstances, however, the pressure in these three mainstems is equal, with the result that there is little exchange of blood among them. Only when occlusion of one or the other occurs does the circle of Willis assume functional importance. Because these anastomoses are not completely adequate, acute occlusion of one carotid significantly lowers the pressure beyond the point of block and therapeutically offers a means of lessening the strain upon aneurysms along that distribution, or of partially reducing the effects of an arteriovenous communication.—Seymour S. Kety, Circulation and Metabolism of the Human Brain in Health and Disease, *The American Journal of Medicine*, February 1950.

PHYSIOPATHOLOGY AND COURSE OF POLYCYTHEMIA VERA AS RELATED TO THERAPY

WILLIAM DAMESHEK, M.D.
Boston

I. INTRODUCTION AND POSSIBLE ETIOLOGIC FACTORS

Polycythemia vera in its numerous manifestations and course lends itself readily to a discussion of physiopathologic principles. Fundamentally, the disease may be considered as a disorder of the bone marrow characterized by an excessive production of blood cells by all the marrow elements, i. e., the nucleated red cells, the granulocytes and the megakaryocytes. To use Greek terms, there is panmyelopathy, which in turn results in pancytosis. The cause of the great and continuous blood production is obscure, but its results lead to many diverse manifestations which, as they are better understood, should lead to better control of the disease.

A large body of knowledge has accumulated in recent years relating to the various substances required for erythropoiesis. Thus, iron, "liver extract factor" (now almost certainly vitamin B_{12}), certain other constituents of the vitamin B complex, including folic acid, certain amino acids and probably many other substances are required to produce red blood cells. When they are lacking, various types of "deficiency" anemias develop which can be corrected only by supplying the appropriate deficient substance. It is well to remember that when such substances are administered, they do not stimulate blood formation; they simply add necessary growth factors which bring about normal cell growth.

Little is known of the actual factors which stimulate cell growth. Loss of blood, either through hemorrhage or by excessive destruction (hemolysis), appears to be a powerful stimulatory factor to the bone marrow since the immediate reaction is an outpouring of early red cells (reticulocytes), granulocytes and platelets. Another stimulatory factor, which, however, affects only the red cells, is that of anoxemia or arterial unsaturation. Whether due to high altitude or to certain types of pulmonary or cardiac disease, there is a resultant increase in erythropoiesis. From the teleologic standpoint, the increased erythropoiesis which takes place with hemorrhage, hemolysis or anoxemia is readily understood although the exact mechanisms by which such stimulation takes place is unknown. Does hemolysis, for example, liberate a stimulating substance? If this is the case, how is one to explain the results of hemorrhage in which blood is actually lost outside the circulation?

If stimulatory factors are so little known, even less is known of possible inhibitory factors although it seems likely that they too are present. Were it not for such "homeostatic" factors, bone marrow growth might conceivably develop out of all proportion to the needs of the body. Certain indications are present implicating the spleen as a bone marrow "regulator" or inhibitor, but actual proof of such substances in splenic extracts is thus far lacking. We must conclude that although the bone marrow probably has normal stimulants and inhibitors which balance each other, thus resulting in extraordinarily stable blood counts, their nature is obscure.

Read before the Section on Pathology and Physiology, at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

From the Ziskind Research Laboratories (Hematology Section) of the J. H. Pratt and New England Centre Hospitals and the Department of Medicine, Tufts College Medical School.

In polycythemia vera, all "stops" to blood production in the bone marrow seem to have been pulled. The marrow is crowded with great numbers of nucleated red cells and granulocytes in all stages of maturation and with megakaryocytes actively producing platelets. Because of their large number and their size, the megakaryocytes often dominate the marrow picture (fig. 1).

What causes this enormous productivity of the marrow? Hemorrhage and hemolysis are not present, and in fact the hemolytic index in polycythemia may be reduced.[1] There is no evidence of anoxemia—cyanosis is lacking, and the arterial saturation is normal. Some observers have claimed that a local anoxemia affecting only the marrow might be present and have pointed to arteriosclerotic lesions in the marrow as evidence of this.[2] This may well be a mistaken cause and effect

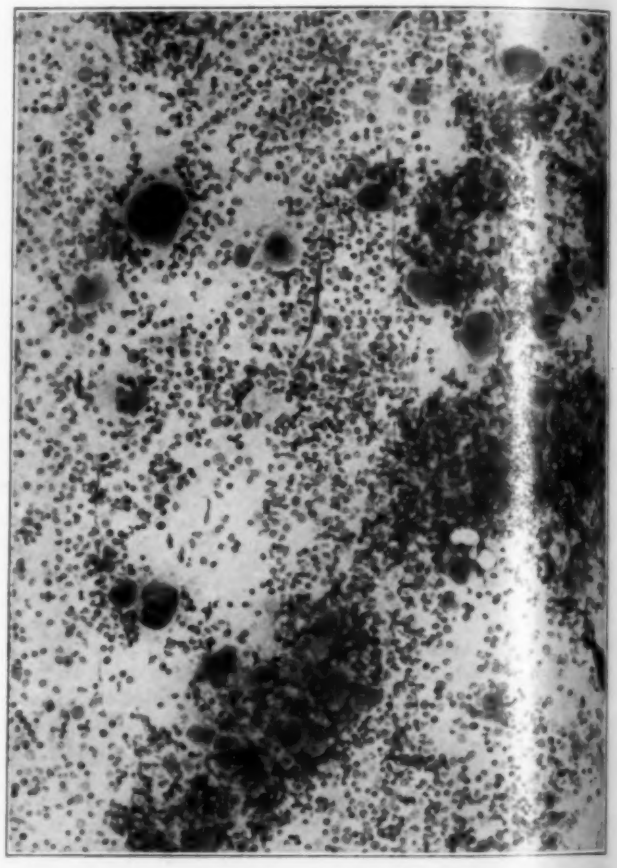


Fig. 1.—Marked megakaryocytic hyperplasia in the bone marrow of a patient with polycythemia vera. Puncture aspiration of the sternum; × 250.

relationship, and the reverse might even be true, i. e., the polycythemic state may lead to early arteriosclerosis. What is even more important, anoxemia leads only to an increase in red cells and not to leukocytosis or thrombocytosis.[3]

Other observers have claimed that polycythemia can be likened to leukemia,[4] i. e., that it is a generalized

1. Miller, E. B.; Singer, K., and Dameshek, W.: Use of the Daily Fecal Output of Urobilinogen and the Hemolytic Index in the Measurement of Hemolysis, Arch. Int. Med. **70**: 722 (Nov.) 1942.

2. Reznikoff, P.; Foot, N. C., and Bethea, J. M.: Etiologic and Pathologic Factors in Polycythemia Vera, Am. J. M. Sc. **189**: 753, 1935.

3. (*a*) Loman, J., and Dameshek, W.: Plethora of the Intracranial Venous Circulation in a Case of Polycythemia, New England J. Med. **232**: 394, 1945. (*b*) Hurtado, A.; Merino, C., and Delgado, E.: Influence of Anoxemia on Hemopoietic Activity, Arch. Int. Med. **75**: 284 (May) 1945.

4. Minot, G. R., and Buckman, T. E.: Erythremia (Polycythemia Rubra Vera): the Development of Anemia; the Relation to Leukemia: Consideration of the Basal Metabolism, Blood Formation and Destruction and Fragility of the Red Cells, Am. J. M. Sc. **166**: 469, 1923. Minot, G. R., and Castle, W. B.: Yearbook of Medicine, Chicago, The Yearbook Publishers, Inc., 1949, p. 398, editorial footnote.

proliferative disorder involving the red cells. This can hardly be likely, for not only is polycythemia vera a chronic disorder without any evidence of invasiveness, but it is a total marrow disorder in which erythrocytosis, leukocytosis and thrombocytosis are all simultaneously present. Neoplastic growth is scarcely like this. Nevertheless the possibility cannot be ruled out that polycythemia vera may be a relatively benign, noninvasive and generalized proliferative disorder of the entire marrow. It has been postulated that endocrine disturbances of pituitary or adrenal origin may result in increased erythropoiesis.[5] This undeniably occurs in certain grossly abnormal conditions involving these glands, in which an erythrocyte count of 5,500,000 to 6,500,000 per cubic millimeter may be present but the white blood cells and platelets are not affected. There is furthermore no evidence of an endocrine dysfunction in polycythemia vera. A possible hereditary or transmitted tendency may be present, since the disorder occurs most commonly in Jews of Russian and Polish origin.[2] Actual familial polycythemia is rare, however.[6] This leaves two highly speculative possibilities: one, the presence of excessive bone marrow stimulation by an unknown factor or factors, and, two, a lack or a diminution in

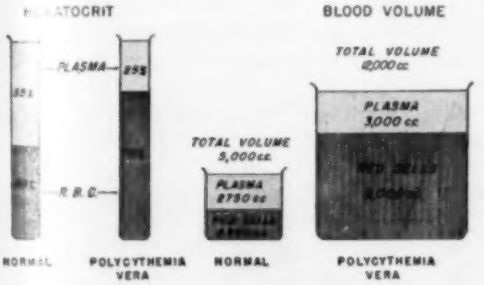


Fig. 2.—Diagrammatic representation of percentage volume of packed red blood cells (hematocrit) and of blood volume in polycythemia vera as compared to the normal.

the normal inhibitory factor or factors. Complete ignorance must be admitted at this time of the cause of true polycythemia and of its exact nature.

II. THE DISEASE

For whatever reason it is present, the panmyelopathy results in an enormous increase in blood cells. All the elements are affected, with the result that the red blood cell count, the polymorphonuclear leukocytes and the platelets become increased. Individual cases of polycythemia differ greatly, not only from the standpoint of how many blood cells are being produced but in the relationship of the three different marrow elements to each other. For example, some cases show only a moderate elevation in erythrocytes, with, however, an extreme degree of thrombocytosis, while in others the leukocyte count may be at or close to leukemic levels, with only slight increases in red blood cells and platelets. The blood counts in polycythemia vera show the ranges given in table 1.

It becomes necessary to define polycythemia vera further. The normal red blood cell count in persons at or near sea level may reach in males the figure of 6,000,000 per cubic millimeter. Certain nervous, high-strung persons with cold, acrocyanotic hands and feet or with peptic ulcer or hypertension may habitually show red blood cell values of 6,000,000 to 6,500,000 per cubic millimeter. Persons such as these do not show an associated leukocytosis or thrombocytosis, and the blood volume is uniformly normal; in fact, the plasma volume may even be low, indicating possibly some degree of hemoconcentration. It is possible that the erythrocytosis in such cases is on the basis of imbalance of the autonomic nervous system.

A sharp distinction must furthermore be drawn between true polycythemia and anoxemic or secondary polycythemia. Polycythemia vera is a panmyelopathy of unknown origin; anoxemic polycythemia is symptomatic of or secondary to various conditions in which

TABLE 1.—*Blood Count Range in Polycythemia Vera*

Hemoglobin	100 to 160% (15.6 to 25.0 Gm.)
Red blood cells	6,500,000 to 12,500,000 per cu. mm.
White blood cells	8,000 to 50,000 per cu. mm.
Platelets	1,000,000 to 6,000,000 per cu. mm.
Reticulocytes	1 to 6%
Polymorphonuclear cells	75 to 90%
Metamyelocytes	5 to 15%
Myelocytes	0 to 5%
Nucleated red blood cells	0 to 2%
Hematocrit	55 to 80%
Mean cell volume	70 to 95 cu. microns
Mean cell diameter	7.0 to 7.5 microns

TABLE 2.—*Differential Clinical and Laboratory Features in Polycythemia Vera and Secondary Polycythemia*

	Polycythemia Vera	Anoxemic or Secondary Polycythemia
Fundamental situation	Hyperplastic panmyelopathy	Anoxemia
Etiology	Unknown	Anoxemia { Altitude, Cardiac, Pulmonary }
Bone marrow	Excessive erythroleukothrombocytopoiesis	Excessive erythropoiesis
Clinical	Plethoric appearance; no pulmonary abnormality; splenomegaly and hepatomegaly; no clubbing of fingers	Cyanosis; chronic pulmonary or congenital cardiac abnormality (cor pulmonale) except in altitude sickness; no splenomegaly; clubbing of fingers
Blood	Pancytosis; erythrocytosis; leukocytosis; polymorphonuclear cells increased; band forms increased; thrombocytosis	No pancytosis; erythrocytosis; white blood cells normal or low; polymorphonuclear cells, band forms and platelets normal
Blood volume	Very high	High
Red cell volume	High	High
Plasma volume	Normal or increased	Low
Arterial oxygen saturation	Normal	Diminished

anoxemia is present. The differential clinical and laboratory features are presented in table 2.

The most important end result of the extreme degree of panmyelopathy in polycythemia vera is the development of an enormous mass of red blood cells in the circulation. The percentage volume of packed red blood cells (hematocrit) in relation to the total amount of blood becomes increased greatly, reaching levels of 60 to 70 per cent or even 80 per cent. But this simple increase in red cell concentration is in itself insufficient to cope with the continued great production of red blood cells (fig. 2). As a result, the total volume of blood becomes expanded to double or triple the normal values. Parallel with this increased volume, the hematocrit continues to rise, so that finally the total red cell mass, which is normally about 45 per cent of 5,000 cc. (2,250 cc.), may become increased in some cases to 75 per cent of 15,000 cc. (11,250 cc.) or to an amount of four or five times the normal!

5. Günther, H.: Ueber die Beziehung endokriner Organe zur Entstehung der Polyglobulie und über klinische Typen hormonal bedingter Polyglobulie, Endokrinologie **4**: 96, 1929.

6. Various cases of "benign, familial polycythemia" (Spodaro, A., and Forkner, C. E.: Benign Familial Polycythemia, Arch. Int. Med. **52**: 593 [Oct.] 1933) that have been reported are almost certainly examples of Mediterranean anemia (hereditary leptocytosis with hypochromic erythrocytosis).

The plasma volume in such circumstances may remain normal or become slightly increased. In the hypothetic examples given the plasma volume becomes increased to 3,750 cc. even though the percentage of plasma is only 25 as against the normal percentage of

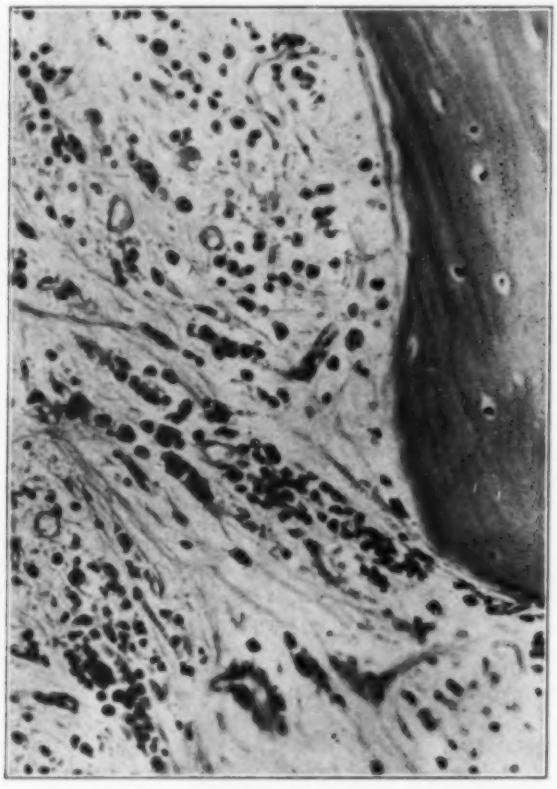


Fig. 3.—Fibrosis of marrow occurring as a terminal event in a case of polycythemia vera.

55. The great increase in red cell mass leads to an abnormal type of physiologic state and thus to a host of clinical symptoms and signs.

III. PHYSIOPATHOLOGY AND SYMPTOMS

The presence of a great mass of blood in the circulation has at least three outstanding effects: (1) plethora, (2) decreased velocity of blood flow and (3) increased viscosity of the blood. The person with polycythemia vera is actually "bursting with blood."[7] All the various organs become distended with a superabundance of blood, and as a result symptoms referable to all the organs of the body develop.[8] This is particularly true of the brain, which is enclosed in the "closed box" of the skull.[8a]

The greater the hematocrit level, the slower is the velocity of blood flow and simultaneously the more viscous the blood. Slow blood flow and increased blood volume may mimic the symptoms of cardiac decompensation. Slow blood flow may also result in disturbances of the extremities, particularly of the feet. The combined effects of a sluggish blood flow, increased viscosity and the very high platelet level are undoubtedly responsible for the thrombotic manifestations which occur so commonly in polycythemia vera.

Peripheral vascular lesions are most common, but coronary thrombosis, cerebral thrombosis, mesenteric thrombosis, hepatic vein thrombosis (Chiari syndrome) and even portal vein thrombosis may occur. Thrombotic disturbances of the stomach may be the cause for the rather common finding of gastric ulcer. This was present in about 1 of every 5 of the cases observed by my colleagues and me. The peripheral vascular lesions may simulate exactly those of thromboangiitis obliterans, especially since both polycythemia and thromboangiitis appear most commonly in Russian and Polish Jews.[2]

Arteriosclerosis appears to be more common in persons with polycythemia than in others of comparable age groups. This may be due in part to the increased blood mass and the sluggish blood flow. Other degenerative disturbances including nephritis and diabetes appear to be more common, diabetes particularly so. In some patients marked nervousness, depression, irritability, increased sweating, increased warmth and loss of weight develop, and the condition thus simulates hyperthyroidism closely. The basal metabolic rate may be distinctly increased in these cases, but the hypermetabolism is of the nonthyrogenous variety and is perhaps due to the great overproduction of blood cells, as in the hypermetabolism of chronic lymphocytic leukemia.

IV. COURSE

Whatever the cause of the constant and excessive hematopoiesis is, it is likely that if the patient lives long enough and does not succumb to the effects of thromboses or other complications, the marrow will gradually show signs of diminished activity. If this

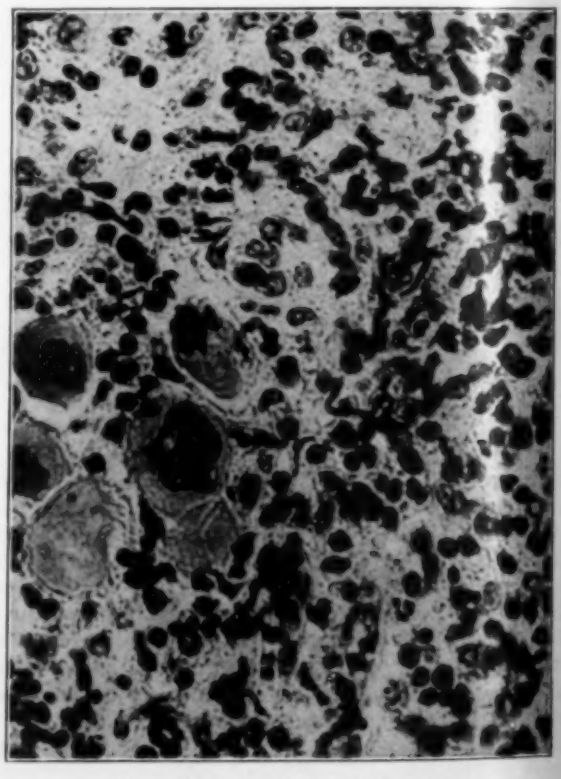


Fig. 4.—Myeloid metaplasia of the spleen.

occurs, the red cell elements become reduced in number and a certain degree of fibrosis develops. With increasing reduction of erythropoietic tissue, myelofibrosis becomes more striking, until in extreme cases the marrow becomes an organized mass of fibrous tissue. This may be due in part to an actual proliferation of fibrous tissue. Leukocyte production, at first

7. Osler, W.: Chronic Cyanosis with Polycythaemia and Enlarged Spleen: A New Clinical Entity, Am. J. M. Sc. **126**: 187, 1903. A Clinical Lecture on Erythraemia (Polycythaemia with Cyanosis. Maladie de Vaquez). Lancet **1**: 143, 1908.

8. Dameshek, W., and Henstell, H. H.: The Diagnosis of Polycythemia, Ann. Int. Med. **13**: 1360, 1940.

unaffected, also becomes reduced, but megakaryocytes usually remain and are unusually conspicuous in the lack of other cell types. The blood smear shows nucleated red cells, increased polychromatophilia and immature granulocytes of various types. This is the "leucoerythroblastic" anemia of Vaughan,[9] the terminal "leukemic" picture of polycythemia described by various authors,[10] Hickling's "non-leukemic myelosis" [11] and Jackson, Parker and Lemon's "agnogenic myeloid metaplasia." [12]

The continued myelofibrosis either results in or is associated with (it is not clear which) extramedullary hematopoiesis in the spleen and to a lesser extent in other organs (figs. 3 and 4). The spleen becomes extraordinarily large and in some cases occupies almost the entire abdominal cavity. It is made up largely of metaplastic marrow tissue (myeloid metaplasia).

The excessive immaturity of the white and the red cells in the circulation is perhaps due to the lack of the normal regulatory effect of the spleen in the presence of myeloid metaplasia involving that organ. It is possible that the spleen acting as "marrow" can no longer regulate the appearance of early red and white cells in the blood with the result that a certain number of myelocytes and normoblasts appear.

Continuing myelofibrosis leads to increasing anemia and finally to increasing leukopenia, granulocytopenia and thrombopenia. The anemia, at first benefited temporarily by transfusions, becomes uncontrollable, especially as hemorrhages due to platelet deficiency supervene. Finally the patient succumbs.

The course of the patient with polycythemia vera (fig. 5) is usually a matter of many years, although it is difficult to state what the "normal" course of the disease would be without the various therapeutic methods which undoubtedly influence it.

The cause of the hemorrhagic diathesis of polycythemia is obscure. Bleeding does not ordinarily occur spontaneously but only in response to trauma as with a blow or following operative procedures. Extreme degrees of postoperative hematomas are common, and excessive bleeding occurs after dental extractions, tonsillectomy, polypectomy and similar procedures. In view of the high platelet levels, the lack of any well demonstrated abnormality of the coagulation factors in the blood and the lack of any apparent abnormality of the capillaries, the cause of hemorrhagic tendency is obscure. In relapse, the bleeding might be explicable on the basis of "bursting with blood," so that when an outlet is made, the blood simply pours out. However, patients often bleed severely when the red cell mass has been greatly reduced.

Certain it is that if a patient with polycythemia requires operative intervention, this should not be carried out lightly. Particular attention must be paid to hemostasis and to the use of local hemostatic materials. The use of fresh whole blood or plasma transfusions with or without added fibrinogen in the attempt to control the hemorrhagic tendency is of value when a major surgical procedure is under consideration. In a case requiring hysterectomy observed recently, 1,000 cc. was first removed by venesection, and then the patient was given a transfusion of fresh, whole blood before operation and another transfusion during operation. No unusual bleeding took place, and postoperative hematomas did not develop.

V. TREATMENT

The treatment of polycythemia vera is a long term project. It is best to consider the polycythemic patient as fundamentally normal. As such, he may have a long life span and every attempt should be made to keep the treatment as physiologic as possible. Since the fundamental difficulty in polycythemia is the extreme overproduction of blood by the cells of the bone marrow, which leads to an excessive mass of blood within the circulation, the treatment may be based either on a diminution of marrow production or on the removal of the excessive blood from the circulation.

Reduction in marrow activity may be carried out by means of either chemicals or roentgen rays. Arsenic (potassium arsenite solution)[13] benzol [14] and, more recently, nitrogen mustard [15] have been used. High voltage roentgen ray therapy either directed over the bones or given in the form of spray irradiation has been used since about 1915.[16] Spray therapy has often induced prolonged remissions.[17] More recently, Erf and Lawrence [18] introduced radioactive phosphorus as a means of administering roentgen ray (beta ray) activity to the cells of the bone marrow. Excellent remissions lasting from three months to three years have been obtained.[19]

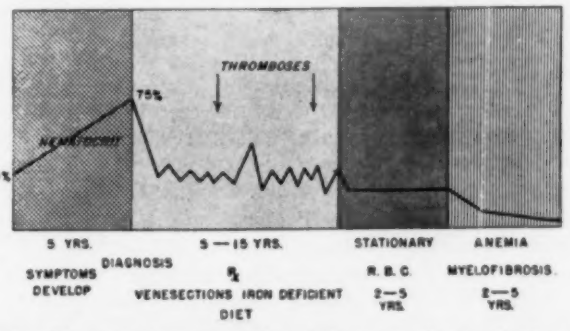


Fig. 5.—Diagrammatic representation of the course of polycythemia vera in some cases. The marrow becomes "burnt out," and anemia develops in about 2 of 10 cases.

The use of roentgen ray therapy and radioactive phosphorus (P^{32}) should be approached with a certain degree of caution. Roentgen rays and radioactive substances when used beyond a rather vaguely defined "safe" dosage are known to have carcinogenic and

9. Vaughan, J. M., and Harrison, C. V.: Leuco-Erythroblastic Anemia and Myelosclerosis, J. Path. & Bact. **48**: 339, 1939.

10. Rosenthal, N., and Bassen, F. A.: Course of Polycythemia, Arch. Int. Med. **62**: 903 (Dec.) 1938. Tinney, W. S.; Hall, B. E., and Giffin, H. Z.: The Prognosis of Polycythemia Vera, Proc. Staff. Meet., Mayo Clin. **20**: 306, 1945.

11. Hickling, R. A.: Chronic Non-Leukemic Myelosis, Quart. J. Med. **6**: 253, 1937.

12. Jackson, H., Jr.; Parker, F., Jr., and Lemon, H. M.: Agnogenic Myeloid Metaplasia of the Spleen: A Syndrome Simulating Other More Definite Hematologic Disorders, New England J. Med. **222**: 985, 1940.

13. Forkner, C. E.; Scott, T. F. M., and Wu, S. C.: Treatment of Polycythemia Vera (Erythremia) with a Solution of Potassium Arsenite, Arch. Int. Med. **51**: 616 (April) 1933.

14. Kiralyfi, G.: Das Benzol in der Therapie der Polyzythämie, Virchows Arch. f. path. Anat. **213**: 399, 1913. McLester, J. S.: Benzol in the Treatment of Polycythemia Rubra with Report of a Case, J. A. M. A. **62**: 1381 (May 2) 1914.

15. Wilkinson, J. F, and Fletcher, F.: Effect of β-Chlorethylamine Hydrochlorides in Leukemia, Hodgkin's Disease and Polycythemia Vera, Lancet **2**: 540, 1947.

16. Sgalitzer, M.: Röntgenallgemeinbestrahlung bei Polyglobulie, Fortschr. a. d. Geb. d. Röntgenstrahlen **46**: 90, 1932.

17. Richardson, W., and Robbins, L. L.: The Treatment of Polycythemia Vera by Spray Irradiation, New England J. Med. **238**: 78, 1948.

18. Erf, L. A., and Lawrence, J. H.: Clinical Studies with the Aid of Radioactive Phosphorus: III. The Absorption and Distribution of Radio-Phosphorus in the Blood of, Its Excretion by, and Its Therapeutic Effect in Patients with Polycythemia, Ann. Int. Med. **15**: 276, 1941.

19. Erf, L. A.: Radiophosphorus, As the Treatment of Choice in Primary Polycythemia, Am. J. Med. **1**: 362, 1946. Hall, B. E.; Watkins, C. H.; Hargraves, M. M., and Giffin, H. Z.: Radioactive Phosphorus in the Treatment of Polycythemia Vera: Results and Hematologic Complications, Am. J. M. Sc. **209**: 712, 1945. Reinhardt, E. H.; Moore, C. V.; Bierbaum, O. S., and Moore, S.: Radioactive Phosphorus As a Therapeutic Agent: A Review of the Literature and Analysis of the Results of Treatment of One Hundred and Fifty-Five Patients with Various Blood Dyscrasias, Lymphomas, and Other Malignant Neoplastic Diseases, J. Lab. & Clin Med. **31**: 107, 1946.

leukemogenic activity.[20] Whether or not the amounts of roentgen ray activity as administered in the ordinary dose of P^{32} used in the treatment of polycythemia are harmful or productive of leukemia is not known. Statistics regarding the development of leukemia in cases of polycythemia, either untreated or treated by various

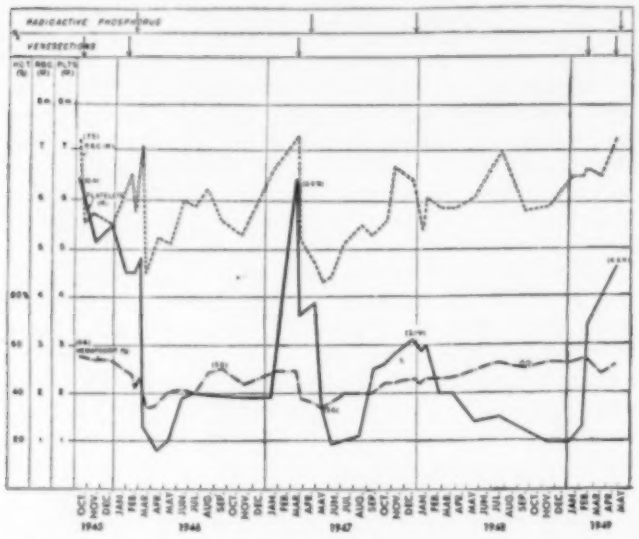


Fig. 6.—Chart of the course in a case of polycythemia vera with extreme thrombocytosis and development of thromboses. The use of radioactive phosphorus resulted in striking reductions in the platelet level and in complete clinical improvement.

measures other than with roentgen ray, are unfortunately meager. They are furthermore confused by the frequent listing as "leukemia" of the leukemoid state of myelofibrosis with myeloid metaplasia.

In my own experience of about 50 reasonably well followed cases of polycythemia, acute leukemia developed in only 1 instance without previous roentgen ray or radioactive phosphorus therapy. Among approximately 100 patients treated at the Mayo Clinic without roentgen rays or radioactive phosphorus acute leukemia is known to have developed in 1. However, in 4 patients of 170 treated with radioactive phosphorus at the same institution acute leukemia developed and

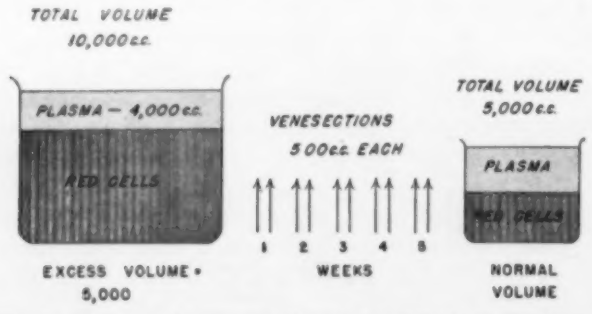


Fig. 7.—Diagrammatic representation of the plethoric blood volume in a case of polycythemia vera and its correction with systematic venesections performed twice weekly. The venesected blood is used for transfusion purposes.

resulted in death.[21] The statistics of J. H. Lawrence[22] and of Reinhard,[23] using radioactive phosphorus, show a smaller incidence of acute leukemia, which they believe is within "normal limits" for the development of this disease in polycythemia.

Time alone and the comparison of large numbers of well documented cases in which patients were treated with and without radioactivity should determine whether or not this therapeutic method is leukemogenic. In my clinic I have restricted the intravenous use of radioactive phosphorus to those patients with polycythemia having frequent thromboses in the presence of an extremely high platelet count or to patients with an unusual degree of refractoriness to therapy with venesections. The reduction which occurs in the blood platelets in patients with thrombocytosis is satisfactory and usually leads to a prolonged remission with an amelioration in the thrombotic tendency (fig. 6).

The other general mode of therapy in polycythemia involves the removal of the excessive amounts of blood from the circulation either by the induction of excessive hemolysis, as with phenylhydrazine, or by multiple venesections. Phenylhydrazine was for years the medication of choice in the treatment of polycythemia.[24] Because of the difficulty of its control, however, and furthermore because the products of hemolysis are

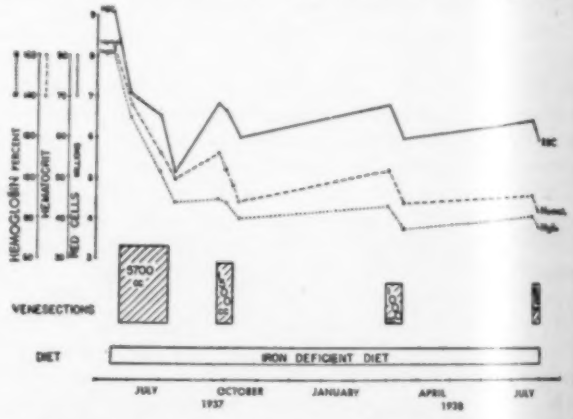


Fig. 8.—Course in a case of polycythemia vera treated with multiple venesections and an iron deficient diet. Note the development of marked hypochromia (discrepancy between the high red cell count and the relatively low hemoglobin value). Complete relief of symptoms occurred with this therapy.

retained within the body, there is an excessive strain on all the avenues of both blood production and destruction. The drug has been well nigh discarded as a therapeutic agent.

The removal of the extra mass of blood by well planned, multiple venesections[25] is productive of two results: (1) the red cell mass is reduced to normal; (2) the bone marrow develops a state of iron deficiency, with the result that the erythrocytes produced are poorly hemoglobinized. The mature red cells, although they may continue to be increased in number, are small and hypochromic and thus greatly reduced in volume.

The reduction of the red cell mass to normal levels is carried out by venesections of 500 cc. which are performed twice weekly. Although estimations of the blood volume are valuable in gaging the extent of venesection therapy, hematocrit determinations are ordinarily sufficient for clinical use (fig. 7). If these are difficult to obtain, hemoglobin estimations are of definite value although they are by no means as helpful as hematocrit levels. Usually the hemoglobin concentrations parallel roughly the hematocrit readings.

20. Ellinger, F.: Lethal Dose Studies with X-Rays, Radiology **44**: 125, 1945. Copp, D. H.; Axelrod, D. J., and Hamilton, J. G.: The Deposition of Radioactive Metals in Bone as a Potential Health Hazard, Am. J. Roentgenol. **58**: 10, 1947. Ulrich, H.: Incidence of Leukemia in Radiologists, New England J. Med. **234**: 45, 1946.

21. Dr. Byron J. Hall, of the Mayo Clinic, supplied these figures.

22. Lawrence, J. H.: Personal communication to the authors.

23. Reinhard, E. H.: Personal communication to the authors.

24. Goodman, L., and Gilman, A. L.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1940, p. 1149.

25. Stephens, D. J., and Kaltreider, N. L.: The Therapeutic Use of Venesection in Polycythemia, Ann. Int. Med. **10**: 1565, 1937. Dameshek and Henstell.[9]

The reduction of the hematocrit level to a normal value of about 45 per cent may require from two to four weeks (i. e., four to eight venesections). With a hematocrit level of approximately 70 per cent, eight venesections are ordinarily required (fig. 8). We have found that the best method of collection is by the use of a no. 16 needle, the flow of blood being facilitated by the use of vacuum bottles. The blood is collected under sterile precautions since it is used routinely for transfusion purposes.[26]

At the end of two to four weeks, longer in some cases, the patient is usually depleted of his extra blood. Because of the rather marked loss of blood in so short a time, fatigue may become noticeable at this point. The considerable loss results in the loss from the body of much of its readily available iron and thus in a state of iron deficiency. Unless there are good reserve stores of iron in the body, or unless there is a continued intake of liberal amounts of iron in the food, this deficiency may be difficult to overcome.

In polycythemia the reserve stores of iron are probably not too great because of the continued need for excessive quantities of iron for production of hemoglobin. In any event the development of a state of chronic iron deficiency is facilitated by the induction of a diet low in iron.

The low iron diet is generally prescribed at the expiration of the course of venesections, i. e., when the hematocrit level has reached approximately 45 to 48 per cent and the hemoglobin level about 85 per cent, or 13.3 Gm. The patient is advised to curtail sharply the intake of foods rich in iron, such as red meats, liver, eggs; certain green vegetables, notably spinach, string beans and Swiss chard; brown cereals (hominy, oatmeal, whole wheat and bran), and shell fish, including oysters, clams and lobsters. To maintain the protein requirements, the patient is asked to drink milk in amounts of 2 to 4 glasses daily, take fish two or three times weekly, chicken or other fowl twice weekly and lamb or veal once or twice weekly with "red meat" not more than once weekly.

The reduction in iron intake leads to an insufficient amount of iron for the synthesis of hemoglobin in the developing red cells, and as a result the mature red cells produced are smaller than normal and occupy less room in the circulation than do normal cells. Production of red cells probably continues in its ordinary rapid fashion, but the insufficiency of iron for the developing red cells results in pronounced hypochromia and microcytosis. Our observations indicate that the iron deficiency state induced by multiple venesections is maintained for longer periods when the patient is on a low iron diet than when he is on a regular diet. At the completion of the venesection period most, if not all, of the patient's symptoms subside, and they do not recur during the length of the remission.

The hemoglobin and hematocrit levels[27] remain low for periods of three to eighteen months or even longer; usually they parallel each other. The red blood cell count, on the other hand, rises gradually after two to three months and may reach levels of 6,000,000 to 8,000,000 within six months or longer. The mean corpuscular volume becomes reduced to levels of 60 to 65 cubic microns, the mean cell diameter from 6.0 to 6.5 microns or less and the mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration to correspondingly low levels. The discrepancy between the high red cell count and the low hemoglobin level (i. e., color index) becomes increasingly more striking. In following a patient in whom venesection has been performed, the hematocrit level and, to a lesser extent, the hemoglobin level are the most important single factors to watch. The red cell count is the least reliable guide to therapy since it fluctuates considerably, and even when it rises to high levels it may have but little significance for the red cell mass.

Within three to eighteen months, or in some cases longer, the hematocrit again reaches distinctly increased levels of above 50 per cent, and at this time the patient usually complains of some of the symptoms previously present, including headache, dizziness and fatigue. At this point two to three venesections may be required to induce a further return of the hemoglobin and hematocrit levels to normal (fig. 7). The amount of blood requiring removal at this time is usually relatively small as compared with that removed during the initial relapse. Representative blood counts in a patient with polycythemia undergoing an iron deficiency regimen are as listed in table 3.

TABLE 3.—*Blood Counts on an Iron Deficiency Regimen*

Beginning of Treatment		At End of Venesection Period	
Hemoglobin	130% — 20.2 Gm.	Hemoglobin	85%
Red blood cells	8,000,000	Red blood cells	5,000,000
Hematocrit	75%	Hematocrit	45%
White blood cells	15,000	White blood cells	15,000
Platelets	1,000,000	Platelets	1,200,000
3 Months Later		**6 Months Later**	
Hemoglobin	85%	Hemoglobin	90%
Red blood cells	6,000,000	Red blood cells	7,000,000
Hematocrit	48%	Hematocrit	52%
White blood cells	10,000	White blood cells	8,000
Platelets	1,000,000	Platelets	1,000,000

It is to be noted that the platelet count remains high and as a rule the leukocyte count also remains somewhat elevated. The marrow continues to show marked hyperplasia, with large numbers of erythroblastic, leukopoietic and megakaryocytic groups. However, the mature nucleated red cells are largely nuclei, with only a small rim of cytoplasm remaining evident.

During the state of chronic iron deficiency the patient himself presents a normal appearance, except that in some cases a brilliant red glossitis develops, due to either iron deficiency or perhaps to a deficiency in the "animal protein factor." Splenomegaly persists.

On this program it is possible to control patients with polycythemia for a few to many years. Some of our patients have been under observation for periods of ten to fifteen years and are in as good health now as comparable persons of the same age group. The course of arteriosclerotic and diabetic manifestations is not affected. We have seen no greater incidence of the myelofibrotic state than in patients with polycythemia treated by other measures.

The disadvantages of the venesection–iron deficiency regimen are (1) the necessity for venesections at more or less frequent intervals, (2) the possibility in the elderly person of inducing rather rapid alterations in cardiovascular dynamics and thus precipitating circulatory collapse and (3) a continued high platelet level with a tendency toward thromboses. For at least 9 of

26. We have used polycythemic blood for transfusions for twenty years and have never seen any ill effects. Polycythemic blood is of unusual value for two reasons: It is unusually rich in red cells and therefore valuable in severe anemia, and its high platelet content is of great value in thrombopenic conditions. After a transfusion of polycythemic blood, the platelet count usually shows a definite increase and full-fledged remissions have not infrequently occurred.

27. The hemoglobin and hematocrit levels usually parallel each other. An approximation of the hematocrit level may be made by dividing the hemoglobin percentage by 2.

10 of our polycythemic patients, however, the iron deficiency regimen has proved to be not only harmless but therapeutically beneficial. Even with the use of radioactive phosphorus, best results are obtained with previous venesections to deplete the great mass of red cells within the circulation.

It must be conceded that all the therapeutic methods for polycythemia at present in use are relatively crude. A more rational approach would be to limit the unknown factors which bring about the excessive blood production. Until these factors are found the therapeutic method used should be both as physiologic as possible and free of immediate and possible future harm.

CONCLUSIONS

1. Polycythemia vera is a disease of unknown origin characterized by an excessive production by all the marrow elements (panmyelopathy), with resultant increases in red cell, leukocyte and platelet counts (pancytosis). Almost all the symptoms of the disease are due to the great increase in blood volume and circulating red cell mass. In addition, there is a tendency for the development of two opposing processes, thrombosis and a hemorrhagic tendency. In about a quarter of all cases sclerosis of the marrow and myeloid metaplasia of the spleen develop.

2. The treatment of polycythemia vera should be as physiologic as possible. For this reason, a systematic venesection–iron deficiency method of therapy is recommended, the use of radioactive phosphorus being reserved for refractory cases and cases of thrombosis.

ABSTRACT OF DISCUSSION

Dr. Paul Reznikoff, New York: The theory of anoxemia of the bone marrow is not dependent on the changes in the larger vessels, the arteriosclerosis, but it is dependent on capillary thickening. Those are difficult to find on section but that is the last vessel where the oxygen exchange takes place between the circulation and the bone marrow tissue itself. Also, I think it is incorrect to consider ordinary polycythemia as a hereditary disease. There is a familial type of polycythemia, but this particular type which we are discussing is not really hereditary unless you conceive of the inheritance of a diet or environment, by which I mean that perhaps the increased incidence of this condition in eastern European people may be due to their particular diet. Askanazy, who was professor of pathology at Geneva, studying vascular changes, showed that the diet in eastern Europe tended to be high in fat or in cholesterol and that the incidence of vascular changes was much greater in eastern European people. The polycythemia or erythrocytosis that occurs at high altitudes is not as extreme, as a rule, as in polycythemia vera, and also often it is transitory. Therefore, I present the hypothesis that perhaps the increase of white blood cells and of platelets is due to the long duration of contiguous irritation in the bone marrow, rather than to a disease involving all three elements. However, that is speculation. The best type of treatment for these patients is the treatment that is most convenient for the patient and that is most efficiently given by the particular physician or the group treating the patient. It seems to me that we hear of just as good results from spray irradiation as from acetylphenylhydrazine. In spite of the dangers of this drug we have been able to keep patients going for long periods with it. Some do not respond well; others lend themselves well to maintenance doses. We have not had enough cases followed for a sufficient length of time to know that one method of therapy is superior to another. Nitrogen mustard has been used by Hayden at the Mayo Clinic over a period of the last year or two with rather spectacular results. We have tried nitrogen mustard in a few patients, and certainly it will have the effect on the blood that the other methods have. What the end result is, we do not know; it has not been used long enough. I agree with Dr. Dameshek that you can use polycythemic blood for your blood bank or for transfusions. We have used it for several years and so far have not seen any bad results. We have been using the blood in the blood blank, and many patients get along quite well with phlebotomies. As Dr. Dameshek has pointed out, roentgen ray therapy is a potent method of treatment. We have used mostly spray irradiation. The average patient received between 100 and 200 r units, and we have had patients go along for five or ten years with only one treatment. Many of them do not, of course; some are refractory to the treatment. Whether radioactive phosphorus may produce excessive damage is at present not known. Certainly we have to consider what the end result may be. The important thing to remember is that polycythemia is not a serious disease, and therefore it is extremely important for us not to treat the blood but to treat the patient. These patients are going along, living fairly comfortably, and it would be a grave mistake if we used drastic agents to have a nice chart rather than to have a happy and healthy patient.

Dr. Paul Klemperer, New York: The basic problem of the pathogenesis of polycythemia vera is still as obscure as it was fifteen years ago when I was interested in the splenomegaly associated with this malady. However, it seems that there is unanimity today in assuming that polycythemia is due to a primary overproduction of red cells and not to a decreased destruction. Dr. Dameshek has referred to the possibility of an obscure form of total marrow stimulation in polycythemia vera. This is in agreement with older beliefs according to which erythremia was compared with leukemia. Today we have much more evidence which speaks in favor of such correlation. The association of polycythemia with increased leukoblastic and megakaryocytic activity has been known for a long time, and the termination of cases of long-standing polcythemia with leukemoid blood changes and anatomic features, indistinguishable from chronic myeloid leukemia, has been repeatedly reported. More recently, the association of polycythemia with leukoerythroblastic anemia has attracted attention. Myelofibrosis and myeloid metaplasia of the spleen, but also of the lymph nodes and liver, are found at autopsy. I have seen at least 3 such cases, with a polycythemic preceding phase, in addition to other instances which first came to observation in the anemic stage. I believe the apparent heterogeneity in these cases and the puzzling features of the blood and tissue changes can be accounted for if one remembers the multipotency of the mesenchymal parent cell of the hematopoietic organs. The developmental potentialities of these cells include not only hematic cell differentiation but also fibroblastic evolution. It is conceivable that even slight qualitative variations of the obscure stimulation of the undifferential mesenchyme may lead to various, often overlapping, states of erythroblastic, leukoblastic, megakaryocytic and even fibroblastic activity which will become manifest as polycythemia, leukemia and leukoerythroblastic anemia with myelofibrosis or osteosclerosis. In regard to Dr. Dameshek's observations on the development of acute leukemia following radioactive phosphorus therapy, I want to mention a similar case of a patient who had been treated since 1939 for polycythemia but only for one year with radioactive phosphorus. Today he is in the ward with a blood count of about 10,000 and 64 per cent blast cells.

Dr. Perk Lee Davis, Philadelphia: At the Lankenau Hospital Cancer Institute we are interested in the use of various modalities, chemotherapeutic in nature, that interfere with cellular enzyme mechanisms. In the last three months we have had 2 cases of polycythemia vera, and it seemed that perhaps we should make use of some of the newer enzyme inhibitors, such as the folic acid antagonists. We have been using amino-an-fol in these 2 cases and have had very good responses so far. The only thing we have not been able to determine in using these inhibitors is whether we will have to have the patients on a maintenance dose and whether, if a maintenance dose will keep them well and hematologically normal, they may then have their meat and their drink, too.

DR. EDWARD H. REINHARD, St. Louis: We have treated 130 patients with polycythemia vera with radioactive phosphorus at Washington University Medical School in St. Louis in the last seven years. Our experience perhaps will enable us to make a suggestion that to a certain extent might reconcile the views that have been presented here. In the 130 patients there have been 2 in whom terminal leukemia developed. We noted that both of these patients had required considerably larger amounts of radioactive phosphorus to control their disease, at considerably more frequent intervals than was true of most of the patients we treated. Our present concept is that perhaps the most satisfactory way to treat the disease is this: The first time a patient with severe polycythemia vera is seen give radioactive phosphorous therapy. Certainly a prolonged remission lasting three, four, five or even six years is obtained from a single course of treatment in some cases. If one observes over several years that the patient has early flare-ups after he has had radioactive phosphorus and if unusually large amounts of radioactive phosphorus appear to be required to control the polycythemia, then it would seem logical to switch to some perhaps less dangerous form of therapy. We advocate the use of radioactive phosphorus therapy routinely until one discovers whether or not the disease can be controlled over a long period of years with only an occasional course of treatment. If this is not possible and if one finds that he is using doses of radioactive phosphorus which perhaps are more than he would like to give, then one can always switch to the other forms of therapy, such as phlebotomy. We have not tried the use of folic acid antagonists, but it would seem that the use of these over a prolonged period would be much more dangerous than the use of radioactive phosphorus. The folic acid antagonists are extremely toxic, and I can see no possible justification for using this form of therapy in a disease which is as relatively benign as polycythemia vera.

DR. F. W. S. MODERN, Van Nuys, Calif.: I should like to report a treatment which I employed in 1 case. The patient was a 40 year old white man who had about 7,000,000 red cells and 11,000 white cells. He was admitted to the hospital because of a peptic ulcer syndrome. The gastric acidity was between 150 and 160 units. We treated him for about ten days with continuous gastric suction, followed by radiation of the stomach from four portals, carefully screening out the spleen. After this treatment within about a month his red cell count dropped from 7,000,000 to about 4,500,000 cells and his white cells from 11,000 to 6,000 or 7,000. The gastric acidity dropped from 150 to 60 units of free acid. We had an opportunity to observe this case for about five years, without relapse. I mention this treatment for whatever it may be worth.

DR. JOHN LAWRENCE, Berkeley, Calif.: In this condition, leukemia is a common and natural complication. Minot and Buckman in 1923 reported that about 20 per cent of their patients developed leukemia, but they did not give a complete follow-up, so there were undoubtedly more. Duncan Graham in Toronto in 1940 reported that 24 per cent of his patients with polycythemia developed a leukemic picture, and the Mayo Clinic group reported in 1943, in a series of 163 patients, the development of this complication in about 17 per cent. Dr. Nathan Rosenthal, who has a tremendous amount of data on this question, has observed in his patients a very high incidence of leukemia. I have seen several patients with polycythemia and leukemia or a leukemoid reaction prior to treatment with venesections, radiation or any other form. There is no evidence that P^{32} has increased this complication, nor has it caused it to disappear. In our series of 150 patients with polycythemia vera, 5 have died of leukemia and 3 of them had been treated by roentgen ray or phenylhydrazine prior to therapy with P^{32}. In the literature there is no correlation between the development of leukemia and any particular type of therapy. With reference to Dr. Klemperer's remarks regarding the multipotential possibilities of these cells, we have observed 2 cases of polycythemia associated with multiple myeloma, and 3 have been reported in the literature prior to treatment with any form of radiation. To decide the best method of treatment for polycythemia vera, we need to answer the following questions: What effect does the treatment have on the patient's comfortable and natural life? How long will it prolong his life? There are two articles which answer these questions in part. One is the report by Richardson and Robbins (Richardson, W., and Robbins, L. L.: The Treatment of Polycythemia Vera by Spray Irradiation, *New England J. Med.* **238**:78 [Jan.] 1948), in which they studied 30 patients with polycythemia vera treated by spray irradiation and found an average age of 64 years at death. The other article is by the Mayo Clinic group (Tinney, W. S.; Hall, B. E., and Giffin, H. Z.: Prognosis of Polycythemia Vera, *Proc. Staff Meet., Mayo Clin.* **20**:206 [Aug.] 1945), who reported a series of 163 patients, 36 of whom lived more than five years. In our experience over a ten year period with polycythemia vera treated with P^{32} the average duration of life after onset is 16.3 years and the average age of death 67 years, which is a nearly normal life expectancy.

DR. GEORGE E. WAKERLIN, Chicago: Until we know the pathogenesis of polycythemia vera we ought to consider seriously the use of polycythemia vera cells for transfusion purposes. The fact that several patients have survived for twenty months after transfusion of polycythemia vera cells does not prove that patients might not be harmed by unknown constituents of these cells.

DR. WILLIAM DAMESHEK, Boston: In an experience of more than twenty years we have found that polycythemic blood for transfusion purposes is not only harmless but valuable. Our polycythemic patients represent a "pool" of valuable donor blood. This is particularly rich in platelets and thus of particular value in idiopathic thrombopenic purpura, especially to tide the patient over a critical period. A definite rise in platelet count can be demonstrated when polycythemic blood is used. Polycythemic blood is also rich in red cells, and its use is therefore something like giving a patient two or three transfusions in a relatively small volume of blood. I have never seen any bad results from the use of polycythemic blood. Some physicians fear to use it because of a supposed relationship of polycythemia to leukemia. However, leukemic blood itself has been injected into normal persons, with completely negative results. Dr. Reznikoff has alluded to a familial or hereditary type of polycythemia. In most of the recorded cases this is not true polycythemia but the hypochromic erythrocytosis of certain mild instances of Mediterranean anemia. Concerning the erythrocytosis of high altitudes, Drs. Hurtado and Merino, of Lima, Peru, have studied this type of polycythemia extensively. No evidence whatsoever of white cell or platelet stimulation was found, even in patients who were natives of an area 15,000 feet above sea level. All the evidence is against the contention that polycythemia vera is due to arterial unsaturation, even in such local areas as the bone marrow. Concerning the allegedly high incidence of "leukemia" developing naturally in polycythemia, one has to discriminate sharply between the leukemoid reactions associated with myelofibrosis and true leukemia. Dr. Byron Hall, of the Mayo Clinic, writes me that in a follow-up study of 100 patients with polycythemia vera not treated with roentgen rays or radioactive phosphorus, only 1 patient developed leukemia. I doubt that polycythemia is associated with a 25 per cent incidence of leukemia as Dr. Lawrence pointed out. The etiology of polycythemia is unkown, and for that reason our methods of therapy are apt to be crude. My feeling, contrary to that of Dr. Reinhard, is that venesection should be used first because potentially it is the least harmful and the most physiologic of the various therapeutic methods. It is important to inject a note of caution regarding the use of radioactive phosphorus. Harmful effects, including leukemia, may occur years after exposure to various forms of roentgen ray activity. I do not know for certain that radioactive phosphorus has a potential leukemogenic effect, but I think it is wise to be cautious about its use, which, I think should be restricted for the present to a relatively small group of patients with polycythemia vera. These include patients with thromboses and high platelet levels, those refractory to venesection therapy and those in the older age group with bad veins and a possible circulatory disorder.

PERFORATIONS IN TRANSURETHRAL OPERATIONS

Technic for Immediate Diagnosis and Management of Extravasations

HERBERT R. KENYON, M.D.
New York

Although many vesical and prostatic lesions are best treated by transurethral technics, procedures of this type are plagued by inherent difficulties and complications not encountered in open surgical interventions. Those seen most frequently are separation of the trigone and perforations through the bladder wall, prostatic capsule or urethra. Since the number of transurethral operations is increasing, we must anticipate a corresponding incidence of operative accidents.

Urologic surgeons are well aware of these misfortunes and make every effort to avoid them. However, the possibility that perforation has occurred may either be overlooked or discounted on the basis of wishful thinking. As a result, the most favorable opportunity to correct damage and obviate sequelae may be lost.

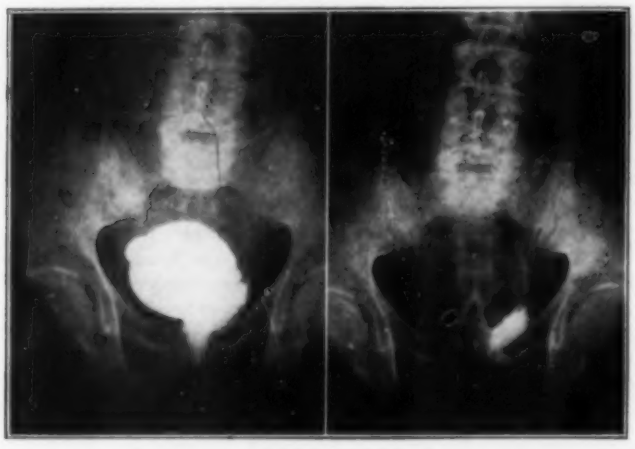


Fig. 1 (case 1).—Cystogram (after removal of resectoscope) showing periprostatic extravasation.

Injuries of this character usually develop during difficult transurethral resections but may complicate litholapaxy, resection of neoplasms or removal of foreign bodies. A few have resulted from sudden overdistention of the bladder by clot evacuators or from the explosion of accumulated gases. Experience proves that the majority of perforations lead to extraperitoneal leakage and that intraperitoneal and combined lesions occur less frequently. Many commentators have described the clinical manifestations of these conditions, and there is general agreement that a bizarre irrigating pattern is usually the first indication of injury. The most serious perforations are signalized by gross interference with free and ample return of the irrigating fluid. Smaller injuries, with little or no obvious impairment of return flow, may escape immediate diagnosis.

Suspicion of rupture should be aroused if abdominal pain develops suddenly during the operation. This occurs even when the patient has received spinal anesthesia and may be inguinal, suprapubic or upper abdominal. The overlying muscles become spastic, and nausea, with or without vomiting, is common. Concomitantly a shocklike state usually develops, with the patient exhibiting pallor, sweating, an increase in pulse rate and a drop in blood pressure. Rarely an initial elevation of blood pressure is followed by a decline to shock levels.

Fig. 2 (case 2).—Immediate urethrocystogram showing site of perforation and extent of extravasation.

These accidents are encountered most frequently as the resection of a lateral prostatic lobe nears completion and the loop reaches the capsule. In resection of vesical neoplasms they usually occur when the base is being excised or coagulated. Deep or excessive coagulation of an actively bleeding venous sinus may result in perforation even when a spherical electrode is used.

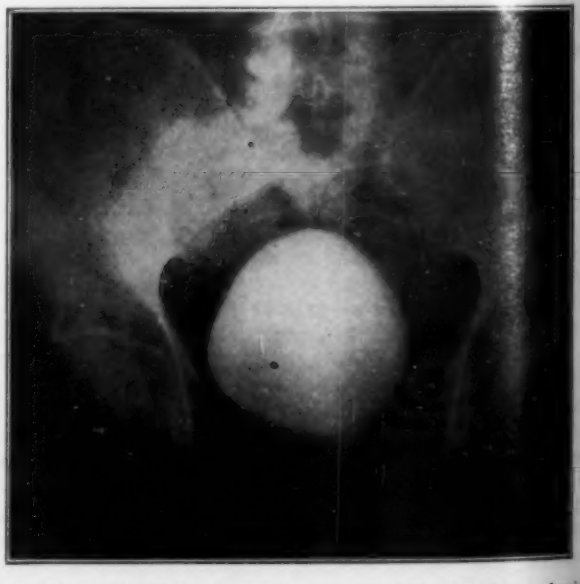


Fig. 3 (case 2).—Follow-up urethrocystogram before discharge showing complete closure of defect.

In 1944 I instituted a regimen that facilitates prompt recognition and diagnosis of accidental perforations.

Read before the Section on Urology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

From the Department of Urology, University Hospital, New York University-Bellevue Medical Center, and the Urologic Service of the Lenox Hill Hospital.

Low spinal anesthesia is employed, with the dose so calculated and administered that little more than saddle anesthesia is obtained. If the patient complains of abdominal pain or the return flow appears to be inadequate at any stage of the operation, it is assumed that perforation is likely. The operation is discontinued and cystography or urethrocystography performed immediately.

Suspicions are thereby confirmed or disproved without delay. Perforation is diagnosed, if present, and the site of the lesion and the extent of extravasation is delineated with precision. Roentgenograms made after evacuation of the bladder often demonstrate the extravasated contrast medium with greater clarity. The type of management selected is determined primarily by the urographic indications. The contrast medium must be sterile and compatible with blood and tissues, requirements that are ideally fulfilled by a concentrated solution of any of the substances used for intravenous urography.

Fig. 4 (case 3).—Immediate urethrocystogram showing site of perforation.

In the early days of transurethral resection Dr. McCarthy and others insisted on the immediate institution of suprapubic drainage whenever perforations were recognized. Anesthesia was continued while the patient was transported to the operating room for emergency surgical intervention. This program resulted in an unduly high mortality as compared with the results obtained in external trauma involving the bladder and urethra. In the latter group, necessary surgical procedures are postponed until shock has been corrected by proper supportive treatment. Since instrumental accidents are almost always accompanied with shock, a similar period of delay and preparation is equally appropriate. I therefore delay secondary surgical measures until the general condition of the patient shows improvement, and I have been gratified by the results achieved. The leakage of urine that continues in the interim appears to be innocuous and without appreciable effect on recovery. When urography demonstrates a localized extraperitoneal extravasation, satisfactory drainage can be maintained solely by urethral catheter in many instances.

A Foley catheter, 22 to 24 French in caliber, with a 5 cc. balloon is introduced with a stylet, which minimizes the possibility of further damage to the prostatic bed or extravesical placement of the catheter. Topical thrombin is instilled if necessary. A larger balloon with traction might be indicated in an occasional case. Irrigations are withheld unless drainage is impaired and then are performed only by the surgeon or a resident. Sterile saline solution, in quantities not exceeding 60 cc. is the preferred irrigant. Occlusion of catheters by clots or debris has been surprisingly infrequent, considering that, because of the interrupted operation, complete hemostasis has not been accomplished.

Fig. 5 (case 3).—Residual contrast medium after evacuation of bladder.

Fig 6 (case 3).—Follow-up urethrocystogram showing restoration of urethral continuity and persistence of right lateral lobe.

Appropriate antibiotic and chemotherapeutic substances are administered routinely before operation and continued afterward as long as necessary. These agents provide a safety factor when perforations occur, and the success of the nonoperative method depends in no small degree on their antibacterial efficacy. The postoperative course in these patients differs little from the

pattern observed in uncomplicated cases except that a longer period of drainage is necessary.

The catheter is removed after six to seven days. Hospitalization is continued for an additional two to three days, during which the urinary pattern is studied. Urethrocystography is repeated before discharge, if feasible. Roentgenograms thus obtained have invariably established the integrity of the injured organ. In none of the patients treated in this manner have perivesical or periprostatic abscesses developed, although these possibilities are never discounted until convalescence is complete.

REPORT OF CASES

The following case reports demonstrate the application of these principles in actual surgical practice.

CASE 1.—S. S. was admitted in September 1945 with benign prostatic hypertrophy and moderate lateral lobe enlargement. Transurethral resection was performed with the patient under low spinal anesthesia. Perforation was suspected because of abdominal pain, drop in blood pressure and suspicious impairment of return flow. An immediate urethrocystogram demonstrated periprostatic extravasation with residual medium present after evacuation of the bladder (fig. 1). An indwelling catheter, penicillin and sulfadiazine therapy were used for seven days. The postoperative course of the patient was afebrile with complete recovery and normal urinary control. To date no complications have been observed.

CASE 2.—J. H. was admitted in October 1946 for benign prostatic hypertrophy with moderate lateral lobe enlargement. Transurethral resection was performed with the patient under low spinal anethesia. The operation was uncomplicated until the capsule on the left was reached. Pain in the abdomen with rigidity and shock developed, together with slight impairment of return flow. A urethrocystogram demonstrated extraperitoneal, periprostatic extravasation (fig. 2). Urethral catheter drainage and antibacterial therapy were continued for eight days

Fig. 7 (case 4).—Bladder tumor. In the cystogram the arrow points to a small area of extravasation.

and followed by normal function and control. Urethrocystography three days later outlined an intact urethra and bladder (fig. 3).

CASE 3.—B. K. was admitted in October 1947 with benign prostatic hypertrophy. Transurethral resection was performed with the patient under low spinal anethesia. Perforation occurred during coagulation of a capsular vein with the ball electrode and was characterized by abdominal pain, slight drop in blood pressure, nausea and vomiting. Immediate urethrocystography showed a subvesical, periprostatic extravasation (figs. 4 and 5), which was treated by urethral catheter drainage and antibiotics. The postoperative urethrogram (fig. 6) showed an intact lumen. The catheter was removed on the eighth day. Initial stress incontinence improved after six weeks' treatment.

Fig. 8 (case 4).—After evacuation of the bladder the defect is more prominent.

When the patient was readmitted eight months later for herniorrhaphy he had normal control, normal urine and occasional nocturia.

In the presence of extensive perivesical extravasations or intraperitoneal involvement suprapubic drainage is essential. A urethral catheter is introduced as soon as the diagnosis is made, but irrigations are withheld and the patient is treated supportively. After four to six hours, improvement is usually satisfactory and any necessary surgical measures can be undertaken with comparative safety. Not only should cystostomy be adequate but all retroperitoneal areas involved in the extravasation should be exposed and drained. Peritoneal defects are closed without drainage after evacuation of the extravasated material. In borderline situations it is safer to divert the urine suprapubically than to rely on the urethral catheter alone.

The following cases represent instances in which the foregoing principles were applied clinically:

CASE 4.—E. D., a woman, was operated on March 12, 1949 for vesical neoplasm. Repeated prior operations—both suprapubic and transurethral—had been performed for multiple recurring papillary neoplasms of the bladder. During coagulation of a tumor near the bladder dome, perforation was suspected. Immediate cystography showed perivesical, extraperitoneal extravasation (fig. 7). The location and extent of lesion was best seen in the residual films (fig. 8). The site of extravasation was confirmed by suprapubic exploration after a four hour period of preparation. Recovery was uneventful.

CASE 5.—F. S. was admitted in July 1945 with a diagnosis of vesical neck obstruction and prostatic calculi. On July 23 transurethral resection was discontinued because of active bleeding. The report of the pathologist showed prostatic cancer. A second resection was performed July 30 at 11 a. m., with the patient under low spinal anesthesia. Bleeding was excessive, but 20 Gm. of tissue was removed. While the surgeon was incising the sphincteric region in its left upper quadrant, abdominal pain developed in the patient, associated with impaired return flow.

The blood pressure dropped from 150 systolic and 88 diastolic to 70 systolic and 40 diastolic, returning to 110 systolic and 60 diastolic after use of phenylephrine hydrochloride (neosynephrine hydrochloride®) and an infusion of sterile saline solution. Persistent vomiting developed. The resectoscope was removed, and urethrocystography showed extensive periprostatic and extraperitoneal extravasation (fig. 9).

An indwelling urethral catheter was placed, which drained fairly well. Penicillin and sulfadiazine were administered together with pantopon® (total alkaloids of opium as soluble hydrochlorides) and intravenous fluids. By 8 p. m. of the same day the general condition was improved. Suprapubic exploration with the patient under general anesthesia showed a rent at 2 o'clock on the sphincter with an accumulation of periprostatic and perivesical fluid and blood clots. This region was drained by Penrose tubes, and the bladder was closed around a suprapubic tube.

Intermittent suprapubic drainage persisted and on Aug. 30, 1945 (one month later) residual prostatic tissue was visualized cystoscopically. On September 10 a third resection was performed without complication, and three days later the suprapubic sinus healed. On September 30 a bilateral orchiectomy was performed. The patient was partially incontinent for seven months but ultimately regained satisfactory control. He was well and working three and one-half years later.

Roentgenologic studies are invaluable when, because of an unusual clinical course, perforation is suspected some time after completion of a transurethral operation. Urethrocystography is performed in bed if the patient cannot be moved. Films made with a portable x-ray apparatus provide useful information and facilitate accurate diagnosis. Hours of doubt and distress, associated with futile attempts to restore drainage by irrigations, are obviated and definitive treatment may be instituted promptly as indicated by the radiographic observations. This is exemplified by the following case.

Fig. 9 (case 5).—Immediate urethrocystogram showing extensive periprostatic and perivesical leakage.

CASE 6.—Y. L., a Chinese man, had a transurethral resection for benign prostatic hypertrophy performed at 2 p. m. Oct. 10, 1944. Complications were not noted until three hours later. At this time abdominal pain developed. Simultaneously the return flow during irrigations became irregular and mild shock was noted. A bedside cystogram showed moderate subvesical extravasation (fig. 10). Irrigations were discontinued, and sedation and a small blood transfusion were administered. Three hours later, at suprapubic exploration, the cystographic observations were confirmed by the identification of a subtrigonal defect. Cystostomy and perivesical drainage were followed by uneventful recovery.

Fig. 10 (case 6).—Bedside cystogram made several hours after resection showing bilateral subvesical extravasation.

COMMENT

The procedure suggested herein provides a rapid and accurate means by which accidental injury can be diagnosed. Essentially, recognition of the perforation depends on awareness and alertness. When doubt exists, I rely primarily on urography. Since most transurethral operations are performed with the patient on a cystoscopic table equipped with x-ray, the prompt performance of urethrocystography requires little effort. The addition of contrast medium to the fluid already present in the extraluminal spaces does not increase shock or tissue irritation.

Drainage by urethral catheter is sufficient when the perforation is favorably situated and the extravasation is limited in extent. There has been no troublesome postoperative bleeding despite the abrupt cessation of the transurethral procedure. In some instances the functional results have been satisfactory even though remnants of prostatic tissue have been left.

Perivesical and periprostatic infections, always a possibility with closed drainage, have not occurred but are always considered as possibilities. These complications have been prevented by maintenance of adequate levels of chemotherapeutic and antibiotic agents.

Morbidity and mortality are lessened in the presence of extensive extravasation associated with shock when supplementary suprapubic surgical intervention is postponed until supportive therapy has been effectively employed. Urographic methods are valuable diagnostic procedures not only in operative accidents but in any situation arising in the course of urologic surgery in which luminal continuity is questionable.

745 Fifth Avenue (22).

ABSTRACT OF DISCUSSION

DR. DEAN MAKOWSKI, New York: The diagnosis and management described by Dr. Kenyon should not be limited to transurethral procedures but should be considered also for unsuspected extravasations due to either direct or indirect trauma to lower abdominal and/or perineal areas. In the past three years at Bellevue Hospital it has been possible to diagnose all cases of suspected urethral or vesical injuries by urethrography and/or cystography. Evidence has been obtained with use of less than 300 cc. of contrast mediums. If anteroposterior views appear normal or a bizarre cystogram results from clots or diverticula, oblique roentgenograms should be taken. In borderline cases interpretation of wet films is misleading. Early operative intervention is advisable once the diagnosis is made. The waiting period of recovery from initial shock can be shortened by intravenous administration of fluids, plasma or whole blood. At Bellevue for the past ten years there were 23 cases of ruptured bladder—not instrumental. Two patients had combined intraperitoneal and extraperitoneal tears, 4 extraperitoneal, and 3 intraperitoneal. Six of the 9 patients died (66.6 per cent mortality). Of these 6, 4 had extraperitoneal rupture (1 had associated injuries, having fallen under a train), 1 intraperitoneal, and 1 combined intraperitoneal and extraperitoneal injury. Of the 14 patients having general surgical and urologic injuries, 3 died (21.4 per cent mortality). Two of the 3 injuries were intraperitoneal and 1 extraperitoneal. It appears that extraperitoneal rupture is no less serious than the intraperitoneal. Early surgical intervention is indicated in both forms of injury. The safest procedure in vesical injuries is immediate cystotomy. Patients with intraperitoneal rupture should have supplementary drainage in the form of a Penrose drain into the lower peritoneal cavity. The use of a modified rubber hemostatic bag which I described elsewhere (*Journal of Urology*, **48**: 126 [July] 1942) will readily locate the laceration and facilitate suturing of it over the distended bag as a guide. This technic will shorten the operating time and decrease morbidity.

DR. LEON HERMAN, Philadelphia: Dr. Kenyon's advocacy of spinal anesthesia is timely. When the bladder has been ruptured during resection the clinical picture is unmistakable if the patient is conscious and the anesthesia low. When the patient has epigastric pain followed by mild shock one should drain the paravesical spaces. I would lack the courage to depend on catheter drainage. In the delayed cases of insignificant extravasation catheter drainage may suffice, but if the local symptoms persist incision with drainage is certainly the safest procedure.

DR. HERBERT R. KENYON, New York: In my paper I deliberately excluded traumatism due to an external injury because the diagnostic procedures involved therein are well recognized. Most physicians working in the urologic field have used cystography for a number of years in injuries of external origin. I am in full agreement with Dr. Makowski in regard to the importance of operating on these patients at the proper time. In the majority of these cases I consider the suprapubic approach superior. I have also found his distensible bag useful for inflation of the ruptured bladder. Provided the urethra is not torn across and the balloon can be readily introduced, it enables the surgeon to identify the bladder with a minimum of dissection of the perivesical tissues. With regard to Dr. Herman's remarks relating to catheter drainage in cases of surgical trauma, when I suspect that an instrumental perforation of the bladder has occurred I have the same feeling of dismay that anyone would experience in like circumstances. However, I have shown incontrovertibly that in certain cases, particularly when it is possible to delineate the lesion accurately and to demonstrate that it is limited in extent, catheter drainage used in combination with newer forms of antibacterial therapy is entirely adequate. I am also of the opinion that a great many perforations probably occur in which the amount of extravasation is so slight that there is no shock and no perceptible interference with the return flow. As a consequence, the possibility of perforation is not even suspected. This may account for some otherwise unexplained hemolytic reactions. If it were feasible to perform urethrocystography at the end of every transurethral resection, I believe that the number of unsuspected perforations that occur and that heal with catheter drainage alone would be surprising.

Clinical Notes, Suggestions and New Instruments

PULMONARY EMBOLISM FOLLOWING INJECTION OF PENICILLIN IN OIL AND WAX

MORRIS AXELROD, M.D.
Brooklyn

Little attention has been given to the possible danger of accidental intravasation of penicillin-oil-wax preparations. I propose herein to report a recently observed case of pulmonary embolism following an injection of penicillin in oil and wax (Romansky formula). A review of the literature indicates that only 2 such cases have been previously reported [1] and that both patients recovered.

REPORT OF CASE

History.—B. G., a man aged 57, was first seen as an office patient on July 5, 1949. The presenting complaints were severe shortness of breath and productive cough of four days' duration. He had consulted a physician twenty-four hours after the onset and was told that his lungs were congested as a result of heart disease. He was given digitoxin and a low sodium diet and advised to rest in bed. The dyspnea became progressively severer. The sputum was blood-tinged on the second day, then becoming mucoid and more profuse. Further questioning added the following pertinent facts: On July 2, 1948 he received an injection of penicillin in the right buttock at a department of health venereal clinic. This was the final injection of a series of fifteen given once a day for the treatment of a syphilitic condition. The injection was received in a standing, slightly flexed position. As the injection was completed and the patient bent down to pick up his trousers, he noted a peculiar salty taste in the mouth and a choking pain in the neck. A severe cough started immediately and persisted. The patient remarked to the physician that "he felt as if the injection had backed up." He was told to rest on a bench and was assured that the reaction was allergic in character. After an hour he felt well enough to leave for home.

Subsequent communication with the clinic revealed that in 1926 he had a penile lesion which was cauterized by a physician. In 1941 reaction of the blood to a routine Wassermann test was 4 plus, and the patient was given two years of intensive therapy with bismuth compounds and arsenicals. In February 1949, when he reappeared at the clinic, the reaction of the blood to the Kahn test was 4 plus. Fluid obtained by a spinal tap on March 28, 1949 showed 10 cells per cubic millimeter. The total protein was 34.5 per hundred cubic centimeter, and the blood gave a plus-minus reaction to the Kahn test. Penicillin therapy was instituted on June 16, and a daily dose (except Sunday) of 600,000 units (2 cc.) of penicillin in oil and wax (Romansky formula) was given with a disposable type plastic syringe.

Physical Examination.—There was pronounced dyspnea and cyanosis. The temperature was 100.2 F. rectally. The blood pressure was 120 systolic and 70 diastolic. The positive observations were confined to the lungs and nervous system. The lungs showed dulness, diminished breath sounds, moist rales and rhonchi over both lower lobes. The heart was normal.

Neurologic Examination.—The right pupil was greater than the left, and both reacted to accommodation but not to light. Except for the pupillary observations, there was no involvement of the cranial nerves. The biceps jerks and triceps jerks were equally active. The knee jerks and ankle jerks were absent. Position sense was intact in the toes, but vibratory sensation was lost over both lower extremities below the knees. The Babinski sign was negative.

Laboratory Data.—The result of urinalysis was negative. Examination of the blood July 7, 1949 disclosed 78 per cent hemoglobin, 4,860,000 red blood cells and 26,200 white blood

1. (*a*) Bondy, P. K.; Sheldon, W. H., and Weens, H. S.: Pulmonary Embolism Caused by Penicillin-Oil-Beeswax (An Experimental Investigation with a Report of a Near-Fatal Case), Am. J. Med. **3**: 34 (July) 1947. (*b*) Frankland, A. W.: Embolism After Penicillin-Oil-Beeswax, J. Clin. Path. **1**: 244 (Aug.) 1948.

cells, with a differential count of 18 per cent segmented neutrophils, 3 per cent nonsegmented neutrophils, 13 per cent lymphocytes, 4 per cent monocytes and 62 per cent eosinophils. When the white blood cell count was repeated July 30 there were 7,800 white cells per cubic millimeter, with 47 per cent neutrophils, 39 per cent lymphocytes, 4 per cent monocytes and 10 per cent eosinophils. A sputum examination July 7, 1949 was negative for fat droplets, eosinophils and tubercle bacilli. The electrocardiogram was interpreted as revealing normal conditions. There was no evidence of right ventricular strain pattern or myocardial damage. Roentgenograms of the chest were made (figs. 1, 2 and 3).

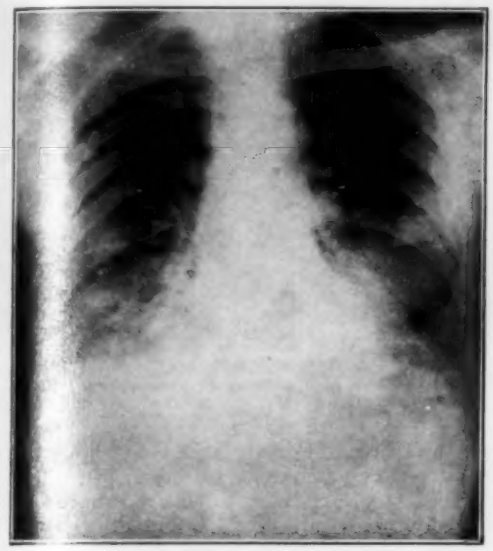


Fig. 1.—Roentgenogram July 5, 1947: Lower halves of both lung fields show irregular areas of decreased illumination.

Diagnosis and Course.—A diagnosis of pulmonary oil embolism was made. The neurologic observations were those of tabetic neurosyphilis, and the spinal fluid observations were consistent with a state of inactivity of the disease. The dosage of digitoxin was discontinued, and the patient was given aminophylline suppositories 7½ grains (0.5 Gm.) twice a day and atropine 1/150 grain (0.4 mg.) orally every four hours. This treatment is indicated in pulmonary embolism to overcome bronchial spasm and bronchial hypersecretion, which occur in this condition.[2] Codeine sulfate was given to control the cough. There was considerable improvement in the condition of the patient in the next few days. On July 12, 1949 auscultation still showed wheezing over both lower lung fields posteriorly. On July 21 the chest was clear clinically. At no time were there any cutaneous allergic manifestations.

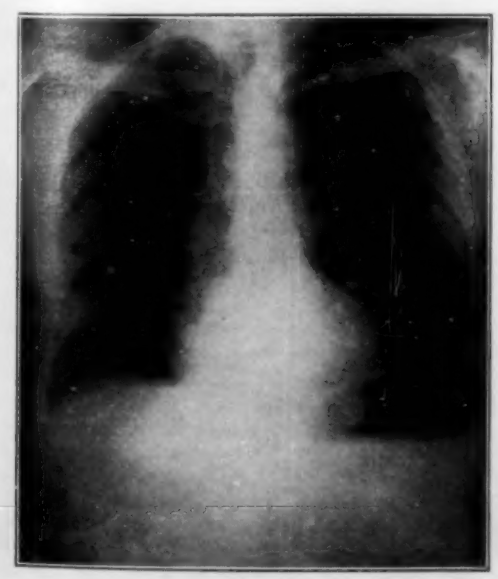


Fig. 2.—July 9: Decided clearing of the lesion with residual involvement in the lower third of the right lung field and lower half of the left field.

COMMENT

The pulmonary reaction to oily substances, whether introduced via the bronchial tree (lipoid pneumonia) or by the intravenous route (oil embolism) depends on the amount and nature of the oil introduced. The response is also believed to parallel the amount of fatty acid which is present in the oil or released by tissue lipase. In pulmonary oil embolism complicating hysterosalpingography with iodized oil (lipiodol,® 40 per cent iodine) the condition is usually mild except when excessively large amounts of iodized oil have been used.[3] Bondy and his associates[1a] investigated experimentally in rabbits the effects on the lungs of intravenously administered penicillin in oil and penicillin in oil and wax. With both preparations they observed in the early stages hemorrhage and edema in the alveoli and cellular infiltration. The animals receiving the drug in oil and wax showed the more decided cellular response, and because of its greater viscosity the material was trapped in the larger pulmonary vessels, whereas the penicillin and oil preparation led to capillary involvement. At a later stage the lesions were similar to those of lipoid pneumonia, namely, granulomatous lesions consisting of a central core of lipoid material surrounded by a polymorphous cellular infiltrate which includes giant cells and esosinophils.

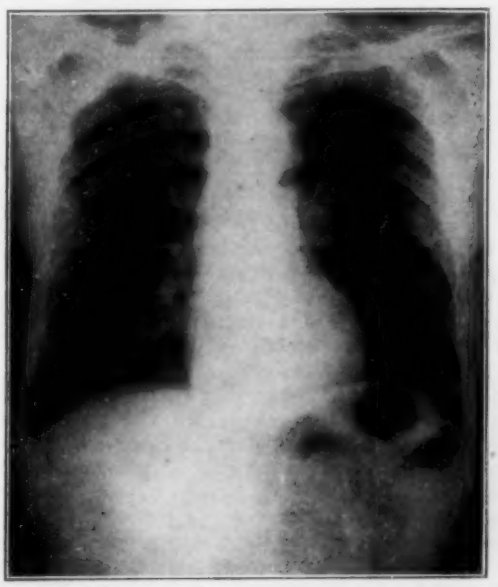


Fig. 3.—Lung fields are clear on July 21. Increased hilar markings are visible on the right side.

There have been no clinical reports of oil embolism following penicillin-peanut oil preparations. The present case and those of Bondy and Frankland were due to penicillin in oil and wax. In each instance 600,000 units of the drug had been injected. The diagnosis should occasion no difficulty. The onset of symptoms follows dramatically the completion of the injection. The patient may notice a peculiar taste in the mouth followed by severe coughing, dyspnea and cyanosis. The sputum is apt to be blood-tinged in twenty-four hours and later mucoid in character. Oil globules may be demonstrated in the sputum in the early stages.[1b] The cough and dyspnea increase in severity until the fourth or fifth day and then begin to subside. Physical examination reveals mainly bilateral rhonchi. Roentgen studies

2. de Takats, G.; Fenn, G. K., and Jenkinson, E. L.: Reflex Pulmonary Atelectasis (in Pulmonary Embolism) J. A. M. A. **120**: 686 (Oct. 31) 1942.

3. Eisen, D., and Goldstein, J.: Lipiodol Intravasation During Utero-Salpingography with Pulmonary Complications, Radiology **45**: 603 (Dec.) 1945.

reveal diffuse, irregular patchy densities in the lower lobes of both lungs. Despite the absence of cutaneous allergic manifestations, the peripheral blood may show decided eosinophilia. Recently Falk and Newcomer [4] described 2 patients receiving penicillin in oil and wax, in whom there developed a clinical picture which the authors considered to fit the designation of Löffler's syndrome. The differentiation of this condition from oil embolism due to penicillin in oil and wax will depend on the roentgen ray and clinical observations. In Löffler's syndrome the pulmonary symptoms are mild or absent and the roentgenogram shows a well defined lesion, generally single, although multiple discrete lesions may be present. Bandy and his associates [1a] noted eosinophilia (10 to 30 per cent) in 10 per cent of patients receiving prolonged treatment with penicillin in oil and wax.

SUMMARY AND CONCLUSIONS

1. A case of pulmonary oil embolism due to penicillin in oil and wax is reported.
2. The clinical features and differentiation of the case from Löffler's syndrome due to penicillin in oil and wax are discussed.
3. The importance of careful aspiration before injection of preparations of penicillin in oil should be obvious.

1836 Ocean Parkway (23).

CERVICAL HERNIA OF THE LUNG

NORMAN VAN WEZEL, M.D.
Foley, Ala.

This case of cervical hernia of the lung is reported because of the rarity of the condition. Until April 1946 there were only 185 cases of hernia of the lung recorded in the medical literature. The majority of these were recorded as a result of traumatic injuries of the chest during wars. Hernia of the lungs may be defined as a protrusion of the pleura-covered lung beyond its normal boundaries through an abnormal opening in the thoracic enclosure.

Hernias are classified according to location, as cervical, thoracic or diaphragmatic. They are also classified (Morel-Lavalleé [1]) according to etiologic factors as congenital or acquired. The acquired hernias may be traumatic, spontaneous or pathologic.

Congenital hernias occur primarily because of anomalies of development with defects of the bony or soft tissue structures of the chest wall. They may be apparent at birth but may not make their appearance until later, when the lung has expanded completely. Acquired types of pulmonary hernia are commoner than the congenital types. The traumatic is the most frequent type of pulmonary hernia. It may manifest itself immediately after the trauma or at some later time during the course of repair of the traumatized site. Prolonged steady pressure of the expanding lung or sudden increased pressure, as from violent exertion, may cause the weakened part to give way and permit herniation.

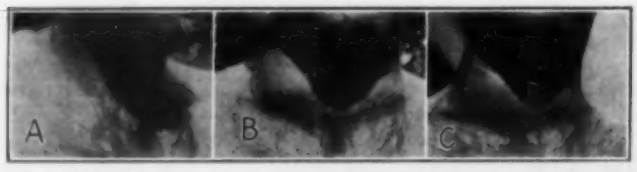


Fig. 1.—Cervical hernia of the lung: *A*, quiet breathing; *B* and *C*, forced expiration.

Spontaneous hernia results from lowered resistance in the thoracic wall which is due to developmental factors plus an abnormal or prolonged increase in the air pressure of the lung. It occurs most frequently in such areas of anatomic weakness as the superior aperture of the thoracic cage and in the intercostal spaces in the anterior chest wall medial to the costochrondral junction of the ribs. Such hernias are observed in patients with chronic cough, chronic severe pulmonary emphysema or in persons subjected to short but severe periods of exertion associated with extreme changes in intrathoracic pressure. The lifting of heavy weights or playing of wind musical instruments may produce it.

In acquired hernias of pathologic origin the thoracic wall has been weakened by some destructive process such as abscess of the chest wall, rib caries or malignant disease. Hernias appearing late after trauma might properly be included in this group because of the probable pathologic changes incident to the healing process.

Fig. 2.—*A*, arrows mark the superior border of the lung during the normal inspiratory phase of breathing; *B*, arrows mark herniation of the lung tissue into the cervical regions on deep expiration and straining.

In 1947 H. Lozar [2] added to this group the oversight of mediastinal hernia. This, too, should be included in the descriptions of hernia of the lung. If so, then there are many hundreds of hernias that are not recorded because they are seen frequently in pneumothorax therapy of pulmonary tuberculosis.

Of all the hernias that are recorded, those of the cervical region are the least common. Maurer and Blades [3] reviewed the literature and found 16 cases of cervical hernias. All these were unilateral, and most were in patients who had a definite history of trauma.

Because of its rarity the following case is being reported in order to add to the literature regarding this rare condition. This case is of greater rarity because the herniation is bilateral and because there is no evidence of trauma.

Cervical hernia usually occurs through the superior aperture of the thorax in the space between the sternocleidomastoid muscle and the scalenus anticus muscle, either as a tear in the traumatic cases or as a deficiency in Sibson's fascia in the congenital group. This case is believed to be a congenital case due to deficiency in the vertebropleural ligament (Sibson's fascia).

REPORT OF CASE

W. W. A., a white man aged 39, a married salesman with two living children, presented himself Feb. 13, 1948 with a history of severe cough, which has been called bronchitis and has become progressively worse each winter for the past six years.

For several weeks he had been coughing more than usual and had noted pain in his right shoulder. It was with the occurrence of this pain that he noted a bulging over the right clavicle. The pain also radiated over the right upper part of the chest. He noticed that the swelling occurred and became larger whenever he coughed, strained or cleared his throat. He had noted the swelling on the left side above the clavicle but had not paid much attention to this. He was actually seeking medical attention because when he coughed the swelling would become so prominent as to break the collar button from his shirt. He smoked one and a half packages of cigarets per day. His family history was noncontributory.

Physical examination revealed normal conditions except in regard to the chest. On straining or coughing there was a definite bulging above each clavicle, which is well demonstrated in the accompanying photographs (fig. 1). On palpation there was definite crepitation over these bulging areas, indi-

4. Falk, M. S., and Newcomer, V. D.: Loeffler's Syndrome—Occurrence in Two Patients Treated with Penicillin in Oil and Wax, J. A. M. A. **141**: 21 (Sept. 13) 1949.

1. Morel-Lavalleé: Hernies du poumon, Mém. Soc. de chir. de Par. **1**: 75-239, 1845.

2. Lozar, H.: M. Bull. V. A. **18**: 319-321, 1947.

3. Maurer, E., and Blades, B.: J.Thoracic Surg. **15**: 77-98, 1946.

cating that they consisted of lung tissue beneath the skin. However, there was no free air or emphysema in the subcutaneous tissue. Pressure could be applied on these without pain. The areas were nontender and could not be held within boundaries when the patient strained. During straining there was no evidence that the bulging was compressing any cervical blood vessels or affecting any nerves.

On a normal inspiratory roentgenogram made with the usual technic (fig. 2*A*), the superior border of the lungs can be seen. On deep expiration and straining, the lung tissue can be seen to herniate into the cervical regions (fig. 2*B*).

COMMENT

The foregoing case is reported for the following reasons: first, cervical hernia of the lung is a rarity; second, because this case of bilateral cervical hernia is, to my knowledge, the first to be recorded, and third, there is no history of trauma.

301 West Laurel Avenue.

ADAPTATION OF THE BURGESS OXYGEN TENT FOR INFANTS

ROBERT DENTON, M.D.
Boston

The administration of oxygen to infants for the relief of anoxia has always been difficult. Adequate therapeutic concentrations of the oxygen have not been obtained with the adult type of oxygen tent, which is tucked under the mattress or rests on the surface of the bedding and which must be opened or raised for nursing care. In my experience, use of the Burgess open top oxygen tent has been the most practical solution of this problem, permitting nursing care without decreasing the oxygen concentration. The Burgess tent is essentially a box of clear plastic material open at the top and with a body opening below. The child's head and trunk are passed through this opening, which is made as air-tight as possible by means of a drawstring. The tent functions satisfactorily and meets all the requirements for oxygen concentration, humidity, accessibility of the patient and simplicity of operation in the treatment of children over 6 months of age.

However, with infants under 6 months of age the following difficulties are encountered: (1) therapeutically inadequate concentrations of oxygen in the tent, usually due to careless closure

Fig. 1.—Usual procedure for setting up Burgess tent.

of the body opening; (2) restriction of respiration by too tight a drawstring; (3) difficulty in removing the infant for feeding, administration of medicaments and other nursing care; (4) difficulty in replacing the infant in the tent after starting parenteral fluid therapy; (5) limitation of the infant's body movements by the drawstring around the trunk, and (6) inaccessibility for physical examination of the chest and abdomen unless the infant is removed from the tent. These faults are real, but they can be corrected by the following simple changes in the procedure for setting up the Burgess oxygen tent:

1. Close the body opening by pulling the drawstring tight.
2. Place a bassinet mattress covered with pliofilm inside the tent to form the floor.

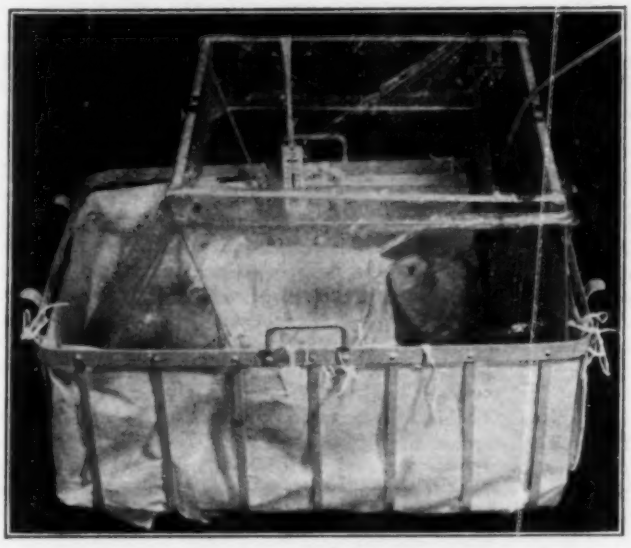


Fig. 2.—New procedure for setting up Burgess tent for small infants. The tent frame rests on bassinet frame, and the mattress is placed inside the tent.

3. Support the tent frame on the bassinet frame as in figure 1.
4. Fasten the tent frame to the sides of the bassinet.
5. Lower the infant into the tent through the top.

Effect of Procedure for Setting Up Tent on Oxygen Concentration, as Determined with Beckman Oxygen Analyzer

Oxygen	Flow Rate (L./Min.)	4	6	8
Oxygen concentration range (%)	Usual procedure	26 to 30	32 to 38	46 to 56
	New procedure	24 to 54	62 to 74	68 to 82

Evidence that this is an improvement on the standard procedure for setting up the tent is shown by the oxygen concentrations in the accompanying table. The infant is easily removed and replaced for parenteral fluid therapy, can be kept in the oxygen tent during feedings, other nursing care or physical examination, and is able to move freely within the tent.

DERMATITIS DUE TO CONTACT WITH IODOACETIC ACID

M. D. MARCUS, M.D.
and
J. B. FRERICHS, M.D.
St. Louis

In the hope of warning those who work with iodoacetic acid, we report 2 cases of dermatitis due to contact with this reagent. In the recent past, there has been considerable increase in the use of this acid in medical laboratories where the Huggins-Miller-Jensen (HMJ) test[1] is being investigated.

Iodoacetic acid is a derivative of acetic acid in which one hydrogen atom is replaced by an iodine atom. In the purified state the acid is a white crystalline substance, molecular weight 185.94, with a melting point of 82 C. Chemically, it is generically related to the chlorine-substituted acetic acids, which are corrosive substances popularly used today for the removal of certain superficial skin lesions.

It is necessary for laboratory personnel to handle iodoacetic acid daily in connection with the performance of the test. Some

From the Department of Medicine, Children's Medical Center. Medical House Officer, Infants' and Children's Hospitals and Children's Medical Center.

From the Departments of Dermatology and Pathology, The Barnard Free Skin and Cancer Hospital.

1. Huggins, C.; Miller, G. M., and Jensen, E. V.: Thermal Coagulation of Serum Proteins, Cancer Research **9**: 177 (March) 1949.

of the iodoacetic acid available today must be recrystallized to obtain the necessary purity, and, while satisfactory pure acid is also available, it is still necessary that fresh solutions of the reagent be prepared daily, thus entailing the handling of the material by the laboratory workers. Apart from such obvious possibilities for contact with the acid as gross spillage in laboratory accidents, it has become evident that even in the careful weighing of the reagent, trivial air currents in the room often transport subvisible particles, which can cause injury to the skin. It is conceivable that similar particles could cause much more serious injury in the event of contact with the cornea.

REPORT OF CASES

CASE 1.—W. C. S., a white man aged 35 and an industrial chemist, had been working for four weeks on the synthesis of iodoacetic acid. On July 12, 1949, while handling purified iodoacetic acid, he removed his rubber gloves for a few moments and noted that some of the material trickled from a test tube onto his fingers. He immediately washed his hands with water. About five hours later his fingers began to burn, and shortly thereafter a bullous eruption appeared on the fingers of both hands. The patient stated that previous contacts with the reagent had occurred, with resultant mild erythematous areas. On July 14, physical examination by one of us (M. D. M.) revealed numerous large, tense bullae, 0.5 cm. to 3 cm. in diameter, on the palmar surfaces of all the fingers and on the palms and wrists. The bullae contained sanguineous and purulent material and were extremely painful. The patient was in a mild state of shock and required large doses of codeine for the

Appearance of the patient's hands ten days after the exposure to iodoacetic acid (case 1).

control of pain. After treatment with warm boric acid packs and the incision of the larger bullae, the process slowly subsided. The roofs of the bullae sloughed, exposing subcutaneous tissues. By August 16 almost complete healing had occurred.

CASE 2.—S. R., a white woman aged 22, is a laboratory worker engaged in the performance of the Huggins-Miller-Jensen test in the laboratories of the Barnard Free Skin and Cancer Hospital. Late in the first day of her experience in handling iodoacetic acid, she noted points of stinging and burning on the exposed portions of her hands, wrists and forearms. That evening she observed small circumscribed areas of erythema, some with small tense central vesicles, in the same locations. The vesicles healed after crust formation, leaving evanescent tiny areas of depigmentation. Only one definite scar occurred, and that followed the deepest of the burns. On several subsequent occasions she observed a similar course of events after exposure to iodoacetic acid, such as occurs when weighing the material. On no occasion had a grossly visible crystal fallen on her skin.

COMMENT

Iodoacetic acid is a caustic chemical which is being increasingly used. Contact with even minute, subvisible particles, such as may inadvertently occur in laboratories, may produce dermatitis. More important, similar contact might well affect the eye. It is probable that the chemical acts as a primary irritant, although the possibility of the existence of a sensitization mechanism has not been ruled out in these 2 cases.

It is suggested that persons handling iodoacetic acid take every precaution to prevent injury to skin and eyes. The most important precautions would appear to be: (1) careful handling of the chemical, (2) prevention of air currents in the weighing room, (3) wearing of rubber gloves, which should be inspected daily for holes and tears, (4) wearing of goggles or spectacles and (5) thorough washing of hands and exposed portions of the arms and face immediately after handling the acid.

CONCLUSIONS

Two cases of dermatitis due to contact with iodoacetic acid are reported. The potential hazards incident to the use of this chemical are exemplified and briefly discussed. Suggestions are made for the prevention of skin, and possible eye, injury from iodoacetic acid.

Council on Foods and Nutrition

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. *In the near future the entire series will appear in book form as the Council's Handbook of Nutrition.*

JAMES R. WILSON, M. D., *Secretary.*

FEEDING OF HEALTHY INFANTS AND CHILDREN

PHILIP C. JEANS, M.D.
Iowa City

FEEDING OF INFANTS

Human milk is the ideal food for the young infant, supplying all the nutritional essentials for the early period with the exception of vitamin D. When human milk is not available, cow's milk is used in substitution. These two foods have different contents of nutritional essentials and different effects on body composition. Comparative contents are shown in tables 1 and 2.

The breast-fed baby who is thriving receives from 2 to 2.5 Gm. of protein for each kilogram of body weight. In the feeding of cow's milk to the young infant it is common practice to supply at least 1½ ounces (44 ml.) of milk for each pound of body weight. This amount is equivalent to 100 ml. for each kilogram and a protein intake of 3.4 Gm. for each kilogram. The larger protein intake of the artificially fed baby is reflected in a greater nitrogen content of the body. This difference is shown in chart 1. After birth the percentage content of nitrogen of babies receiving cow's milk increases in a curve rather smoothly continuous with the curve of prenatal content.[1] When human milk is fed, a sharp change in the direction of the curve occurs after birth and for a time the proportion of nitrogen in the body remains at birth level or decreases slightly.

TABLE 1.—*Approximate Percentage Composition of Human Milk and Cow's Milk* *

Type of Milk	Fat	Sugar	Total Protein	Lactalbumin	Casein	Total Ash	Calcium	Magnesium
Human	3.5	7.5	1.25	0.75	0.50	0.20	0.032	0.004
Cow's	3.5	4.7	3.4	0.50	3.0	0.75	0.118	0.012

Type of Milk	Potassium	Sodium	Phosphorus	Sulfur	Chloride	Iron	Copper
Human	0.041	0.011	0.013	0.014	0.032	0.0001	0.00035
Cow's	0.155	0.050	0.093	0.033	0.105	0.00005	0.00020

* The figures of this table are intended to represent mean values. For compiled ranges for some of these components reference may be made to Jeans, P. C., and Marriott, W. M.: Infant Nutrition, ed. 4, St. Louis, C. V. Mosby Company, 1947.

The breast-fed baby who is thriving receives approximately 0.06 Gm. of calcium for each kilogram of body weight. The artificially fed baby who ingests 100 ml. of cow's milk for each kilogram receives 0.12 Gm. of

Because of limitation of space, the footnotes have not been included in THE JOURNAL, but are included in the Handbook of Nutrition and in the author's reprints.

calcium for each kilogram. The larger calcium intake of the artificially fed baby produces a greater calcium content of the body, as shown in chart 2. With both types of feeding a decrease in percentage of calcium in relation to body weight occurs for several weeks after birth, after which period the percentage content with cow's milk feeding starts to rise, while that with human milk feeding continues to fall for several weeks and probably does not reach the birth value before the baby is 1 year of age. The calcium content of human milk is used more efficiently than that of cow's milk, but the total retention from cow's milk is greater because of the larger quantity fed. The calcium retention of the baby fed cow's milk is as great as or greater than the calcium intake of the breast-fed baby.

The significance of these differences in body composition is not clear. One interpretation could be that a wide range of normal exists and that the differences are of no great significance. The period of time during which the differences exist is short compared with the life span. The differences disappear soon after the differences in diet cease to exist.

While this point of view may be acceptable for the baby born at term, it is inappropriate for the baby

TABLE 2.—*Approximate Vitamin Content of Human and Cow's Milk*

Type of Milk	Average Values for Each 100 Gm. or Ml.					
	Vitamin A, I. U.	Vitamin D, I. U.	Vitamin C, Mg.	Thiamine, Mg.	Riboflavin Mg.	Nicotinic Acid, Mg.
Human *	290	5.0	6.4	0.013	0.04	0.1
Cow's †						
Raw	180	2.5	2.0	0.045	0.20	0.1
Pasteurized	180	2.5	1.1	0.035	0.20	0.1
Evaporated Reconstituted	180	2.5	0.6	0.025	0.20	0.1

* Values for human milk are based on data from Macy, I. G.; Williams, H. H.; Pratt, J. P., and Hamil, B. M.: Human Milk Studies, Am. J. Dis. Child. **70**: 135 (Sept.) 1945.

† Values for cow's milk are based on data from Lawrence, J. M.; Herrington, B. L., and Maynard, L. A.: Human Milk Studies, Am. J. Dis. Child. **70**: 193 (Sept.) 1945.

born prematurely. The chief reasons the prematurely born baby is highly susceptible to rickets are the low calcium and phosphorus content of the body at birth and the frequent failure to supply sufficient of these minerals after birth. Human milk cannot be ingested in amounts sufficient to supply the need unless it is fortified or supplemented with calcium or a calcium-containing food.

In explanation of the high calcium content of the baby fed cow's milk as compared with the baby fed human milk, and with the justifiable concept that human milk is the ideal food, the idea has been advanced that the baby fed cow's milk is supermineralized. Eliot and Park [2] interpreted the results of their study of the bones of newborn babies as indicating that calcium is present in sufficient amount to represent storage. This interpretation was accepted by Hamilton,[3] who expressed the belief that the relative calcium loss in early infancy represents utilization of stores and is normal. After 3 months of age the rate of percentage of calcium increase in the body when cow's milk is fed parallels the fetal rate, a condition which, if it does not represent physiologic normal growth, at least produces storage. Storage to this extent certainly is not harmful, and it may well be considered useful during periods of illness when calcium utilization is impaired. The rate of calcium increase after 3 months of age for the baby fed cow's milk is similar to the rate of increase of ash content of the fat-free animal body as predicted by Moulton.[4]

Linear growth of babies fed a standardized cow's milk formula is related to the amount of calcium retained.[5] The differing retentions with the standardized diet are obtained by varying the vitamin D

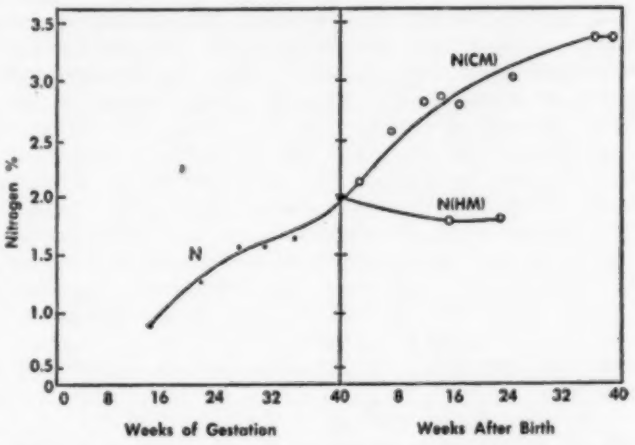


Chart 1.—Changes in relative nitrogen content of fetus and infant. The regression line of nitrogen content of the fetus is drawn from data in the literature. CM, infants fed cow's milk; HM, infants fed human milk. (From Stearns, G.: Physiol. Rev. **19**: 415 [July] 1939.)

intake. Babies with poor retentions grow at average or less than average rates, while those with higher retentions grow at rates greater than average. Thus the higher calcium retentions would appear to be definitely advantageous to the artificially fed infant. On the other hand, the breast-fed baby has excellent linear growth despite a much lower calcium retention and grows at a rate definitely greater than that of the artificially fed baby who has the same calcium retention.[6] It becomes obvious from these and other facts that factors other than those under consideration enter into the rate of growth and that probably it is inappropriate to state requirement standards for the artificially fed baby based on the requirement of the baby fed human milk.

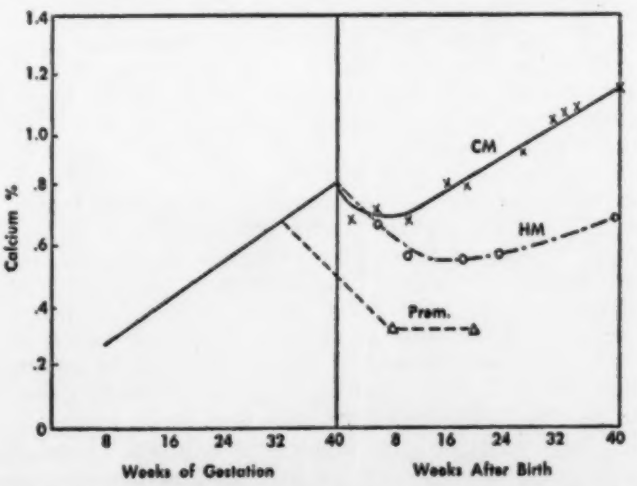


Chart 2.—Changes in relative calcium content of fetus and infant. The regression line of calcium content of fetus is drawn from data in the literature. CM, infants fed cow's milk; HM, infants fed human milk; Prem., prematurely born infants fed human milk. (From Stearns, G.: Physiol. Rev. **19**: 415 [July] 1939.)

The greater nitrogen retention of the artificially fed baby must of necessity represent larger amounts of tissue protein in the body, since nitrogen is not stored in any other fashion. The larger part of the increase

in tissue protein is represented in increase in muscle mass. Babies who are fed cow's milk in the larger of the customary quantities have approximately 25 per cent more muscle mass than breast-fed babies.[7] This increase takes place soon after the artificial feeding is started, after which time the muscle mass maintains a fairly constant relationship to the total body weight. The muscle masses of breast-fed and artificially fed babies increase in a parallel manner, but with larger values for those receiving cow's milk. No disadvantage seems to accrue to the breast-fed baby because of the lesser amount of muscle. On the other hand, nitrogen retentions of the artificially fed baby of the same order of magnitude as those of the breast-fed baby are associated with poorer tissue turgor and poorer motor development than are shown by artificially fed babies receiving the larger amounts of cow's milk and having higher nitrogen retentions. If these observations are correct, cow's milk formulas devised to simulate human milk in percentage composition are not so useful as are formulas containing larger amounts of protein and calcium.

The phosphorus content of the body and the phosphorus requirement depend on the amounts of calcium and nitrogen retained. Consequently the requirement of the baby receiving cow's milk is somewhat greater than that of the infant fed human milk. The phosphorus content of human milk is much less than that of cow's milk, but human milk contains an amount sufficient to meet the needs of the infant relative to the amounts of calcium and nitrogen retained. Cow's milk contains an excess to the extent that much more phosphorus is absorbed than can be used, the excess being excreted chiefly in the urine. Little or no phosphorus is excreted in the urine of the breast-fed baby, whereas in the artificially fed baby 60 to 70 per cent of the total excretion is by way of the urine. The baby seems to accomplish the increased excretion without difficulty or damage.

Human milk is superior to cow's milk as a source of iron. Although human milk contains only 0.5 to 1.5 mg. of iron to the liter, it contains on the average twice as much as does cow's milk. The iron stores at birth are sufficient to permit maintenance of a normal hemoglobin level for several months, after which time additional iron is necessary. After 3 months of age with customary cow's milk formulas the iron retention is variable, but averages approximately zero; when human milk is fed, the average retention is approximately 0.11 mg. Neither of these iron intakes is satisfactory, for a retention of at least 0.7 mg. is required after 6 months to maintain the hemoglobin level.[8] Without additions the body of the baby becomes progressively poorer in iron. The iron content of human milk and its utilization are such that nutritional anemia is much slower to develop in the breast-fed baby than in the artificially fed baby when no iron supplement is given. Possibly also the greater content of folic acid in human milk plays a role.

Whether the baby is breast or artificially fed, special supplements of vitamin A are unnecessary. The requirement for vitamin A is related to body size. The Food and Nutrition Board of the National Research Council has recommended 1,500 units daily at 6 months of age. Even for a baby 1 year of age this amount is greater than that computed as optimum on the basis of weight from experiments with animals when all the vitamin A is ingested as carotene. Thus the amount recommended appears ample. Computation shows that the required amount of vitamin A is supplied by milk alone, either human[9] or bovine,[10] if it is of average content. In the early months the breast-fed baby receives more vitamin A than does the baby fed a cow's milk formula prepared by dilution. In addition to the vitamin A of the milk, the early addition of orange juice makes a small contribution and the subsequent additions of egg yolk, vegetables and fruits permit an intake of vitamin A or its precursors well above the recommended allowance. Clinical observations also have shown that babies receiving a normal standard diet grow equally well whether or not they receive additional vitamin A.[11] Thus for the average baby the important contribution of fish liver oil is vitamin D.

The ascorbic acid content of human milk varies directly with the intake of the mother[12] but in general is relatively large in comparison with the content of prepared cow's milk. An approximate average content of human milk in this country is 50 mg. to the liter, whereas a cow's milk formula prepared by boiling and dilution may contain 6 mg. or less to the day's supply.[13] Thus average human milk meets the standard allowance for vitamin C, whereas the amount in prepared cow's milk is grossly inadequate. Even though the requirement is met by average human milk, the feeding of orange juice to the breast-fed baby is in no way harmful and may be considered beneficial in those instances in which the mother's supply of ascorbic acid is small.

The thiamine content of human milk varies widely and depends on the diet of the mother.[14] Knott and her co-workers[15] found that milk from mothers who supply their infants adequately contains more thiamine than milk from mothers whose babies require a formula supplement. When mothers supplied their babies adequately the milk contained an average of 192 micrograms to the quart; with inadequate supply the average content was 86 micrograms. The larger of these two values was obtained when the mothers received approximately 1.5 mg. of thiamine daily. At times the thiamine content of human milk is less than the requirement of the infant. Clements[16] observed symptoms of partial thiamine deficiency in 8 per cent of a group of 150 breast-fed babies. The thiamine content of the milk was low in each case.

Cow's milk as fed to babies is subjected to heat treatment, which causes significant losses of thiamine as compared with the original milk. Table 2 shows that heat-treated cow's milk contains more thiamine than does human milk. However, cow's milk usually is diluted for feeding the young baby. Even with maximum customary dilution the thiamine intake of the artificially fed baby equals or exceeds that of the breast-fed baby when averages are considered.

The minimum thiamine requirement is approximately 0.24 mg. for each 1,000 calories.[17] Symptoms of deficiency do not appear when this amount is ingested. The thiamine intake should be something more than the minimum requirement. The allowance considered appropriate by the Food and Nutrition Board of the National Research Council is 0.5 mg. for each 1,000 calories or 0.4 mg. daily for a baby 6 months of age. Both average human milk and average dilution formulas for young infants contain only the minimum requirement of thiamine. Thus questions have arisen as to the adequacy of the thiamine intake of the infant. The breast-fed infant, although he has no thiamine to spare, seems to do very well nutritionally. One difference between human milk and formulas of cow's milk is the higher proportion of calories from fat in human milk.

Slightly more than 50 per cent of the calories of human milk are from fat, while the calories from fat in a customary formula often are as low as 35 per cent. Thiamine is not concerned in fat metabolism and fat consequently has a sparing action on thiamine. Therefore the thiamine requirement is more equally met in the two instances than seems apparent. In any case early supplement with thiamine-containing foods is desirable.

With prevention of depletion of body stores as determined by load tests used as the criterion for the riboflavin requirement, approximately 20 micrograms for each kilogram is the minimum requirement for adults.[17] The allowance recommended for adults by the Food and Nutrition Board of the National Research Council is one-third more than this minimum requirement or 26 micrograms for each kilogram. Requirement data for children and particularly for infants are meager. Some implication exists that infants and children may need relatively more than do adults. The Food and Nutrition Board has suggested an allowance of 75 micrograms for each kilogram for the infant, an amount probably higher than it need be.

The riboflavin content of milk depends chiefly on the dietary intake. It varies widely in human milk [18] and to a lesser extent in cow's milk.[19] The average content of cow's milk is approximately five times that of human milk. The young baby who receives practically all his food as human milk gets approximately 65 micrograms of riboflavin for each kilogram. The young baby who receives a customary dilution formula receives at least 160 micrograms for each kilogram. Thus the riboflavin intake of babies receiving cow's milk formulas need cause no concern, and it is probable that the intake of the thriving breast-fed baby is ample even though it does not meet fully the suggested allowance of the Food and Nutrition Board.

Nicotinic acid requirement is directly related to the protein intake at all ages inasmuch as part of this requirement can be supplied by tryptophan. When the tryptophan content of the diet is low, the nicotinic acid need is approximately 10 times that for thiamine; on this basis a suitable allowance at 6 months is approximately 4 mg. and the minimum requirement half this amount. At this age the infant obtains 1 to 2 mg. daily from his milk [20] and relatively little from other food sources. The reason that deficiency symptoms do not occur with a customary diet is that milk is a good source of tryptophan. Both tryptophan and nicotinic acid are necessary for growth.

Neither human [21] nor cow's milk [22] supplies an important amount of vitamin D. The various relationships of the components of human milk, including the calcium to phosphorus ratio, are such that calcium and phosphorus are more efficiently utilized from this food than from cow's milk. Rickets is less common among breast-fed than among artificially fed babies. Nevertheless, breast-fed babies sometimes develop rickets, and the calcium and phosphorus retentions of babies receiving human milk are increased when vitamin D is given. The requirement of the breast-fed baby for vitamin D is not known accurately, but probably it is little or no different from that of the artificially fed baby as discussed subsequently.

In the preceding discussion certain large differences in body composition between breast-fed and artificially fed babies have been mentioned. The significance of these differences to the baby is not clear. Our present knowledge does not seem to warrant the selection of one type of composition as preferable to the others. Detailed nutritional studies have not proved any inferiority of human milk as compared with cow's milk in infant feeding, despite the facts that certain essential components are present in small amount and that well managed artificial feeding produces a type of body composition that might seem more desirable from certain theoretical points of view. The usual reasons advanced for preference for feeding human milk are trite, although largely correct. These reasons pertain to ease of digestion, low bacterial count, relative freedom of the infant from infection, infrequency of digestive disturbances, production of good growth and physical status, infrequency of serious illness, relative ease of diet regulation, relative absence of allergy, avoidance of human error in prescribing and preparing a formula and psychologic satisfaction. It may be, as so often is stated, that nature intended human milk for the human infant and cow's milk for the more robust stomach and more rapid growth of the calf. However, nature has not informed us so clearly as to when other foods should be added to the diet and what foods should be given. For answers to these questions we must depend on empiric practice as modified from time to time by scientific observation. That certain food components should be added early seems clear.

Supplements to the Milk Diet of the Infant.—Ascorbic Acid: Most babies at birth have blood levels of ascorbic acid of at least 0.7 mg. and some 1.0 mg. or more for each 100 ml. of blood.[23] The blood level decreases promptly and rapidly. By the tenth day the artificially fed baby may be expected to have approximately 0.4 mg. for each 100 ml. of blood, an undesirably low level. By the fourth or fifth day the breast-fed baby is receiving ascorbic acid in significant amounts, but in the case of the artificially fed baby the custom of delaying vitamin C administration until the second month is altogether too common. Orange juice, the most frequently used source, even when started late, is commonly given in amounts much too small to meet the need. The young artificially fed baby has been found to need approximately 20 mg. of ascorbic acid daily in addition to the small amount in the formula in order to have a blood value comparable to the lower blood levels of breast-fed babies. Thus at least an ounce (30 ml.) of orange juice is desirable, beginning in the early days after birth. By the time the baby is 3 months old the amount of orange juice given could well be 2 ounces (50 ml.) or even more; 2 ounces supply approximately 30 mg. of ascorbic acid, a suitable allowance for this age period. In the private practice of medicine "intolerance" of orange juice is encountered frequently, but in hospital practice this condition is found most rarely. From the point of view of digestion orange juice is little more than a 10 per cent solution of dextrose, a food that should not disturb the alimentary tract of the most delicate infant. Perhaps it is not a coincidence that babies who cannot tolerate orange juice also have difficulty with tomato juice. For those who are intolerant to these foods, ascorbic acid is widely available.

The prematurely born baby has a need for ascorbic acid greater than that of the baby born at term; vitamin C is necessary for utilization of several of the essential amino acids.[24] The amount usually adequate for this purpose is 50 mg.

Vitamin D: The need for vitamin D from special sources exists from birth. One good argument favoring

the use of milk fortified with vitamin D is that probably no one hesitates to prescribe this type of milk for the earliest formulas, whereas perhaps the majority of physicians wait several weeks or into the second month before prescribing a fish liver oil. Fish liver oils in appropriate amounts may be expected to produce no digestive difficulties at 1 to 2 weeks of age. The condition to be feared most at this early age is lipoid pneumonia produced by aspiration of the oil. It is partly for this reason that some physicians use concentrated preparations of vitamin D in preference to cod liver oil. Other and perhaps preferable alternatives exist. Preparations of both vitamin D_2 and D_3 are commercially available in solutions that are freely miscible with the milk formula and offer the advantage of dispersion of the vitamin, in which state it is more efficiently utilized than in the concentrated form.

The requirement for vitamin D has been set at 400 units daily by the Food and Drug Administration; 400 units is the daily allowance recommended by the Food and Nutrition Board of the National Research Council. No acceptable evidence has been found that a normal infant needs more than 350 units daily for optimum or for maximum calcium utilization when the vitamin D is of no greater concentration than exists in cod liver oil.[25] The prescribing of several times this amount is common practice. Evidence exists that amounts greater than 1,500 units daily are detrimental in that appetite decreases after several months of use, with consequent decrease in calcium retention and in growth rate.[26] One teaspoonful daily of the less potent of the acceptable cod liver oils or ½ teaspoonful of the highly potent cod liver oils is adequate. If preparations of such concentration as viosterol are used, a dosage of 4 or 5 drops is preferable to the 10 drops so commonly used. The dosage of vitamin D should be considered in terms of units; volumes should be stated only in interpretation to the caretaker of the infant in relation to the specific product to be used.

The concept is widely held that the baby born prematurely requires more vitamin D than does the baby born at term. This concept seems to be in error.[27] The increased susceptibility of the prematurely born baby to rickets is due to needs for larger intakes of calcium and phosphorus than often are supplied. The vitamin D requirement is not increased.

Cereals: It is the almost universal custom in this country to prescribe cereal as the baby's "first solid food." The age at which cereal is given to infants has varied with different generations of physicians, but at present addition of cereal to the diet at 3 months is common practice. This current practice finds its counterpart in ancient times and is an empiric custom. Its continuance has been based on the clinical impression and belief that babies thrive better when receiving cereal. Among the cereal products often listed as suitable for infant feeding are farina preparations, foods that presumably add little to the nutritional value of the infant's diet.

Earlier in this review has been mentioned the usefulness of supplementing the milk diet of the infant with foods containing iron and thiamine and possibly other members of the B complex. Whole grain cereals and especially fortified proprietary cereal foods contribute importantly to the satisfaction of these needs. Thus an empiric custom receives support from modern scientific evidence, but only when cereal foods are carefully selected.

It is the custom of a few physicians to defer the feeding of cereals until the second half of the first year and to supply the needed iron and B vitamins from egg yolk, vegetables and fruits. When these foods are given in appropriate quantities the supply of iron and the B vitamins is somewhat greater than from whole grain cereals, although not greater than from some of the fortified proprietary foods. Thus among the natural foods the known needs of the infant are supplied better from egg yolk, vegetables and fruits than from whole grain cereals. When these foods are given, the feeding of cereal loses much of its importance and may be deferred until the capacity of the infant increases to the extent that the entire group of foods can be taken comfortably.

Other Supplementary Foods: Some of the food values of egg yolk, vegetables and fruits have been mentioned in the preceding section. Egg yolk is frequently given, preferably cooked, at 3 to 4 months of age, sieved vegetables at 4 to 5 months and sieved fruits at 4 to 6 months. The giving of a variety of these foods twice a day instead of the usual cereal twice a day not only supplies needed nutrients but helps to accustom the infant to variety in flavors and textures of foods, a goal highly desirable from the point of view of forming good feeding habits.

Meat. Meat preparations excellent for infant feeding are widely available in both sieved and coarser forms. If desired, the sieved meats can be fed at an early age. While meat protein is not an important addition to the milk diet, the meats are good sources of iron and the B vitamins; they are useful also in helping to give variety to the diet in texture and flavor.

Psychology of Infant Feeding.—The psychologic aspects of infant feeding[28] are fully as important as those more obviously nutritional. One of the common complaints relating to children brought to the pediatrician is anorexia, usually dependent on training in feeding habits and usually having its origin in infancy. Often the formula prescription of the physician contributes to the onset of the difficulty. A definite volume of food is prescribed, and the conscientious and solicitous parent endeavors to give this exact quantity of formula at each feeding regardless of possible variations in appetite. In this manner rebellion against food and the parent may have its beginning.

The interrelationships which are set up between mother and child during the early days and weeks after birth set a pattern which is important in determining the type of response the child will have toward eating. Giving and receiving represent the most basic aspect of all social relationships. The infant-mother relationship is the simplest example of a social situation. Attitudes are communicated to the infant from the earliest moments and affect his behavior. The perception of impatience or hostility by the infant heightens the anxiety in him and produces physiologic changes which are not conducive to satisfactory feeding and digestion. Changes in the type of food or manner in which it is given constitute a problem in learning for the infant. Hence, psychologic preparedness for changes should be evaluated by assessment of the infant's mood.

Feeding by both parents is helpful in fostering emotional development. The mother needs the active support of her husband and the doctor. The infant's manual preparedness in feeding develops after 6 or 7 months and should be encouraged so far as is feasible.

Acceptance or rejection of new foods is affected greatly by the attitude of the mother toward those foods. If a mother has a revulsion toward a food, such as cod liver oil for example, communication to the baby of her emotional state is common, with the result that the baby refuses the food. The baby's behavior is modified by the unconscious attitude of the mother. Correction of this fault is difficult.

The so-called self-demand schedule has become fairly common. Much is to be said in favor of having the baby's feeding time when he is most frequently hungry rather than at some time regulated by the clock. Usually such a schedule is regulated by the mother rather than by the doctor, and some common sense is required. Thus the schedule is easily subject to abuse and the baby may be fed every time he cries, a procedure that leads to faulty feeding habits.

The desirability of variety in flavor and texture has been mentioned. These variations should be introduced early. The child who has had only liquid and sieved foods throughout the first year frequently refuses coarser foods when finally they are offered. At least some of the fruits and vegetables offered should be chopped or mashed rather than sieved after the sixth or seventh month. The continuance of bottle feeding after the first year is not good feeding practice and is usually evidence that other environmental factors are faulty.

FEEDING OF CHILDREN

The conclusion is reached easily that the diets of our children have improved in many ways over those of the past. It is clear also that they have not yet improved sufficiently even in those economic levels at which the cost of food is relatively unimportant.

It is customary to attribute increased rate of growth of a population group to improvement in nutrition. Certainly it has been demonstrated that nutrition definitely affects the rate of growth. Whether the cause is wholly nutritional or dependent also on greater freedom from disease and on other factors, studies have shown that young people of this country are taller and heavier than were the children of former years. For example Meredith [29] has shown that boys living in the United States today are 6 to 8 per cent taller and 12 to 15 per cent heavier than was the case half a century ago. He found the size of the boys to be related to economic status. He found also that differences in size were unimportant when related to geographic distribution within the United States.

Other studies have shown that well fed babies and children grow at rates greater than average. Growth rates of babies recorded over the past 25 years show a gradual and definite increase, starting with the data of Baldwin (1921) [30] and progressing through those of Kornfeld (1929),[31] Stuart (1934) [32] and Jackson (1945).[33] Although these differences are greater among infants, they appear also for the child. The assumption seems justified that the increased growth rates are largely attributable to improved nutrition.

Despite improvement in nutrition over the years, much evidence exists that current diets are often unsatisfactory. While the national over-all averages of per capita consumption of food show no deficiency, dietary surveys in families show an unequal distribution of food and nutritional essentials.[34] The nutrients most commonly found deficient are riboflavin, calcium, thiamine and ascorbic acid. Although not often mentioned in this grouping, protein and vitamin D deficiencies also are relatively common in childhood. These deficiencies are discussed subsequently.

Another dietary fault is represented in the occurrence of dental caries. While no consensus exists as to the details of the cause of dental caries or the mechanism of its prevention, whether it is nutritional or oral environmental, or both, it is generally agreed that diet plays an important role. On this basis improper diet is common in childhood, since dental caries is almost universal.

Except for special therapeutic purposes, probably no need exists for special preparations of vitamin A to be given in addition to that present in the diet. Evidence is conflicting concerning the frequency of vitamin A deficiency among the children of this country. Certainly vitamin A is relatively abundant in many of our foods, and any reasonably good diet contains ample not only to meet the minimum requirement but for storage. It is clear also that if a diet is fortuitously deficient in vitamin A, it is deficient also in many other essentials and that much more is needed than the addition of vitamin A alone. It is believed that in a high proportion of instances in which children are found to have clinical evidence of vitamin A deficiency the deficiency is dependent on defects of utilization in greater measure than on dietary deficiency.[35] Infections and illnesses produce prompt response in impairment of utilization. In the continued presence of illness large therapeutic doses of vitamin A may be required to supply the need or these large doses may fail to produce a noticeable effect.

Vitamin D is commonly deficient in the diet of the child. Many children receive an inadequate amount of sunshine in the summer and few receive a sufficient amount in winter. Giving vitamin D preparations has become routine in infancy, but relatively few mothers realize that vitamin D is important throughout the growth period. Without vitamin D children vary widely in their ability to use calcium and phosphorus; for some the utilization is excellent, for others poor. Since distinction between these two types of children cannot be made without prolonged and detailed special study for each child, it is appropriate to consider that all children require vitamin D. When the calcium and phosphorus intakes are adequate and appropriate, 300 to 400 units of vitamin D daily will produce retentions of these minerals ample to satisfy the theoretical requirements for normal growth.

Much circumstantial evidence exists that thiamine probably is obtained by many children in amounts less than those considered appropriate or optimum.[36] The remedy for this situation, to the extent that it exists, lies in a better selection of dietary components rather than in the giving of special preparations of thiamine. In general refined cereal preparations are to be avoided except as they have been enriched. The lower the economic level, the greater the extent to which the energy need is supplied by refined cereal products and sugar, sometimes amounting to 50 per cent or more of the total energy intake. Enriched bread and flour are now generally available. Much ado has been made over the increasing consumption of refined sugar, some believing that sugar is harmful per se, but all agreeing that it is likely to replace foods more valuable nutritionally. Macy [37] has observed that the better the diet from the nutritional point of view, the less the desire of the child for sugar. She concluded that the amount of sugar taken voluntarily by a child is an excellent criterion of the adequacy of the diet. If this

point of view is correct, the point of attack is not to restrict sugar but to improve the diet by increasing the amounts of nutritionally valuable foods offered.

Thiamine is reputed for its effect on the appetite. An important proportion of children for whom parents seek medical advice are brought to the physician because of anorexia. In few of these instances the anorexia is correctible by thiamine medication. Although the child may be receiving suboptimal amounts of thiamine and other essentials, the fundamental difficulty lies in the environment and training in feeding habits, these bad habits often having had their origin early in infancy. The correction of these habits has little relationship to thiamine.

A child who ingests his expected allowance of milk receives from this source alone most if not all of the riboflavin required: For the child who does not receive his quota of milk, the possibility of deficiency not only of riboflavin but of other essentials as well is to be considered, and the diet must be supplemented accordingly in a special and expert manner if it is to be complete. Meat, particularly the glandular organs and lean pork, is a good source of the B group of vitamins. If ingested regularly, it is a better source of thiamine and nicotinic acid than is milk; it is inferior to milk as a source of riboflavin. Eggs contribute importantly to the supply of B vitamins as well as other nutritional essentials and should be included in the diet frequently, preferably daily.

Calcium is the chief mineral requiring attention during childhood, since the other essential minerals are more likely to be present in sufficient amounts in most diets. Milk and milk products are our best food source of calcium. In the case of the young child the usual diet, exclusive of milk, contains approximately 0.2 Gm. of calcium; the diet of the older child contains approximately 0.3 Gm. The remainder of the requirement of 1 to 1.5 Gm. is normally supplied by milk. Thus one may speak of the milk requirement in relation to the calcium need.

A curve of the theoretical requirement for retention of calcium may be constructed by apportioning according to the rates of growth at different ages the total accretion of calcium from birth to maturity. When such a curve is constructed, the daily retention requirement is found to decrease from approximately 300 mg. in infancy to a low point of about 180 mg. early in the preschool period, then to increase to about 450 mg. at the beginning of adolescence.[38] The efficiency of children in calcium utilization varies widely, but when vitamin D is given the range of retention is not great, although always the amount ingested exceeds greatly the amount retained. With respect to the calcium requirement in terms of milk, it has been found that during the early part of the preschool period 1 pint (473 ml.) of milk in addition to the usual diet permits retentions adequate to meet the theoretical retention requirement, which is low at this age.[39] Very quickly after this time and up to approximately 10 years of age the retention requirement is not met until the quantity of milk is increased to 1½ pints (710 ml.) daily. The requirement during early adolescence is a quart (946 ml.) of milk daily. It seems unwise to place any emphasis on the low requirement in the early preschool period. This period is brief, approximately from 2 to 5 years of age. More is received by the baby immediately preceding this period, and more is required subsequently. Milk should not be considered solely as a source of calcium. It contributes most importantly to the requirement for protein as well as other essentials. During the period when the calcium requirement is lowest the requirement for protein is high. Consequently it seems preferable to advise at least 1½ pints of milk after the period of infancy and up to the age of 10 years. The taking of a full quart throughout this period can be considered only as beneficial, provided the larger quantity does not crowd from the diet other essential foods. The fear or belief that the larger quantity may have this effect is widely prevalent but not too well founded, especially for those children who have normal appetites. It is true that in some instances psychologic reasons arise for giving the smaller quantities of milk mentioned as meeting the calcium requirement. In such instances the protein requirement can be met with other protein foods, such as meat and eggs.

Calcium deficiency, at least in moderate degree, is believed to be widely prevalent in childhood. To whatever degree such a situation exists, it is usually much worse during adolescence. At this age period the requirement is increased and too often the intake not only is not increased but actually is decreased, sometimes because of a desire, especially in girls, to remain slim. It is during the adolescent period particularly that dental caries tends to become rampant, a condition believed by many observers to depend in part on nutrition and by some observers to depend to some extent on calcium metabolism.

The custom of prescribing or using calcium salts is widely prevalent. Such salts have a definite field of usefulness in special circumstances, but they have no rightful place in the normal diet. When they are used, they should be chosen carefully for the purpose intended and the dosage should be more nearly adequate than it frequently is. The phosphates of calcium are as well utilized as the same salts in milk. The calcium needs for growth can be satisfied easily by means of these preparations. In order that calcium may be usable for growth, it is necessary that a proportionate amount of phosphorus be available at the same time. The calcium of such salts as calcium lactate and gluconate is utilizable for retention only to the extent that phosphorus is present otherwise in the diet. All diets contain at least a fair amount of phosphorus, but the amount usually is not adequate to permit the best use of the calcium of these salts. The chief objection to the customary use of the calcium salts is that they are not food in the usual sense, and they are often used as a substitute for milk. It is obvious that calcium salts can be a substitute for milk in only a most restricted sense and that the diet must be supplemented in many additional ways in order to compensate for the absence of milk.

The possibility of protein deficiency in the diets of children has received some, but insufficient, attention. One of the criteria which may be used for estimating the protein content of the body is the creatinine output in the urine. Creatinine excretion is directly proportional to the amount of muscle in the body.[40] When children are fed ample protein, the creatinine excretion (consequently the amount of muscle) rises to a constant level for each child, with a narrow range at each age period for a group of children.[41] When these values are plotted according to the age and in terms of creatinine for each kilogram of body weight, a curve is obtained which may be considered as representing normal conditions as regards creatinine output and muscle mass. Creatinine data collected from the literature, as well as data from this clinic, show that the great majority of

children studied have creatinine values below, often considerably below, the theoretically normal curve when they first come under observation. Those with normal values are the exception rather than the rule. In all the instances in which observations have been made the creatinine output increases promptly to the normal level when amounts of protein are fed which are consistent with what are considered standard dietary allowances. It appears that when children receive suboptimum amounts of protein they approach as nearly to the normal creatinine excretion as their protein intakes permit them. It is of interest also that the weight of the child may be, and in fact usually is, within what is considered the normal range when the low creatinine values are observed. The size or weight of the body is not a criterion for judging protein metabolism.

In meeting the protein requirement, one should place emphasis on the value of milk. A quart of milk daily supplies most of the protein need of the young child and half the need at the beginning of adolescence. Such a quantity of milk contributes more protein to the diet than any other single food. When milk is excluded from the diet, the protein requirement of the child can be met only if special and expert supervision is given.

SUMMARY

Despite all our modern knowledge of infant nutrition and all the current refinements of artificial feeding, feeding at the breast of the mother remains an ideal procedure. This is true despite the fact that human milk contains only a bare minimum of most of the nutritional essentials and the fact that the body composition of the breast-fed baby departs widely from that which preceded and that which follows, in contrast to the body composition of the artificially fed baby, which maintains more closely a smooth continuance of the fetal and postinfancy curve.

Vitamin D is needed early by all babies, whether breast or artificially fed. Vitamin C is needed early by artificially fed babies and is a harmless safeguard for the breast-fed baby. Babies born prematurely have a need for vitamin C somewhat greater than that of babies born at term, and this need exists from the time of birth. No need for vitamin A from special sources exists. If current custom is in error, it errs in the direction of giving too much vitamin D and too little vitamin C and in not giving either of these early enough.

Additional supplementary foods should be given at not later than 4 months of age to both breast-fed and artificially fed babies. One important function of these supplements is to supply iron and vitamins of the B group. Another function is to accustom the baby early to variety in flavor and texture for the promotion of good feeding habits. Anorexia and poor feeding habits, which occur so frequently in older children, often have their origin in feeding mismanagement in infancy.

In a general way we have done reasonably well nutritionally for our babies, but not so well for children past infancy. The nutrition of the child has been improved during the past generation, but not to the extent desirable or possible with present knowledge. Although observers do not agree too well as to the particular nutritional or dietary factors responsible for dental caries, nearly all are of the opinion that one or more dietary components may be responsible, either by lack of those which are essential or by the presence of some considered harmful. On such a basis, dental caries is our most widespread nutritional scourge.

At least three nutritional essentials deserve special emphasis in childhood, namely, vitamin D, protein and calcium. Vitamin D is required throughout the growth period, a fact extensively overlooked. Milk as our only constant good food source of calcium is not taken in sufficient quantity by a large number of children. Protein deficiency is much more common than is generally realized. A diet adequate in protein cannot be arranged fortuitously without the inclusion of milk.

Although thiamine is obtained by a large proportion of children in quantities scarcely meeting their needs, the remedy lies in better food selection, not in thiamine medication. Enrichment of flour and bread has contributed materially to the desired end; decreased consumption of sugar also should be helpful.

Vitamin A from special sources is not needed by the normal child. A diet fortuitously deficient in vitamin A is deficient also in other respects. The remedy is a better diet, not medication.

ACCEPTED FOODS

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

The Gerber Products Company, Fremont, Mich.

GERBER'S STRAINED APRICOTS WITH FARINA consists of apricots, farina, sugar and salt.

Analysis (submitted by manufacturer).—Total solids 21.85%, moisture 78.15%, ash 0.61%, fat (ether extract) 0.20%, protein (N × 6.25) 0.91%, crude fiber 0.42%, carbohydrates other than crude fiber (by difference) 19.71%.

Calories.—0.84 per gram; 23.89 per ounce.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	1166 U.S.P. Units
Thiamine	0.014 mg.
Riboflavin	0.014 mg.
Ascorbic acid	1.19 mg.
Nicotinic acid	0.36 mg.
Calcium	11.8 mg.
Phosphorus	21.9 mg.
Iron	2.00 mg.

Use.—For use in the feeding of infants, convalescents and others requiring a soft diet.

GERBER'S STRAINED PEARS consists of pears, sugar and lemon juice.

Analysis (submitted by manufacturer).—Total solids 13.91%, moisture 86.09%, ash 0.24%, fat (ether extract) 0.43%, protein (N × 6.25) 0.32%, crude fiber 1.46%, carbohydrates other than crude fiber (by difference) 11.46%.

Calories.—0.51 per gram; 14.46 per ounce.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	48 U.S.P. Units
Thiamine	0.014 mg.
Riboflavin	0.028 mg.
Ascorbic acid	0.83 mg.
Nicotinic acid	0.22 mg.
Calcium	9.1 mg.
Phosphorus	10.3 mg.
Iron	0.82 mg.

Use.—For use in the feeding of infants, convalescents and others requiring a soft diet.

GERBER'S CUSTARD PUDDING consists of whole milk solids, sugar, egg yolks, arrowroot, white flour, whole eggs, cornstarch, salt, vanilla and water.

Analysis (submitted by manufacturer).—Total solids 21.83%, moisture 78.17%, ash 0.91%, fat (acid hydrolysis) 2.79%, protein (N × 6.25) 3.14%, crude fiber 0.07%, carbohydrates other than crude fiber (by difference) 14.92%.

Calories.—0.97 per gram; 27.60 per ounce.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	180 U.S.P. Units
Thiamine	0.025 mg.
Riboflavin	0.108 mg.
Ascorbic acid	0.92 mg.
Nicotinic acid	0.080 mg.
Calcium	89.7 mg.
Phosphorus	80.1 mg.
Iron	0.29 mg.

Use.—For use in the feeding of infants, convalescents, and others requiring a soft diet.

Committee on Cosmetics

REPORT OF THE COMMITTEE

In view of widespread medical interest in hexachlorophene (G-11, AT-7, K-34) and the intensive advertising associated with it, the Committee has authorized the publication of a status report on the recent adaptation of hexachlorophene as an essential ingredient in deodorant soaps. This information is for the physician to enable him to answer questions on these products.

OFFICE OF THE SECRETARY.

STATUS REPORT ON DEODORANT SOAPS

Intensive promotional campaigns for a new type of product, the deodorant soap, has caused interested observers to ask, "Has an ideal method for controlling body odor been developed?" A deodorant in the form of a soap would be welcomed by those already conditioned to the lathering properties of soap as an indispensable cleansing medium for removing extraneous debris and for controlling body odors. A soap which would deodorize and cleanse could obviate many of the deficiencies of present available methods of inhibiting malodorous perspiration. Advantages claimed for these deodorant soaps include ease of application, greater economy and relative freedom from stained clothing.

The tremendous commercial potentialities of a soap with deodorant properties have been partially responsible for the stimulation of research in this field for a number of years. Much of this research has been based on the assumption that offensive perspiration odor can be controlled by inactivating the bacterial flora of the skin. According to laboratory and clinical investigations perspiration per se is not malodorous, except in a few pathologic conditions. The odor of perspiration becomes offensive only when bacterial activity causes decomposition of the organic material in the perspiration. A large number of effective cream, liquid and powder deodorants have been developed on this principle. Until recently, germicidal substances which maintained both sufficient antibacterial activity when incorporated into a soap and a reasonable degree of safety were not available. However, wartime use of the chlorinated phenol compounds demonstrated properties which gave new impetus to the search for a deodorant soap. These chemicals exhibited rapid antibacterial action on first exposure, cumulative action with repeated use, adsorption on the skin with retention for several days and maintenance of bactericidal and bacteriostatic efficiency when incorporated into a soap. Of these compounds, hexachlorophene (bis[2-hydroxy-3,5,6-trichlorophenyl] methane) is being employed in deodorant soaps.

As these products are newly introduced into commerce, questions are raised concerning safety, pharmaceutic elegance, efficiency and truthfulness of advertising claims. Some pertinent questions on deodorant soaps can be answered at present; others must await further use and experimentation.

With regard to safety, considerable data have been accumulated to support the belief that hexachlorophene (G-11, AT-7, K-34) is nonirritating for practical purposes in the 1 to 3 per cent concentrations commonly employed. Its sensitizing propensities and possible chronic toxic properties cannot be evaluated fully until it has been widely used for a comparatively long period of time. To date, indications are that the sensitizing and toxic properties of hexachlorophene in the concentrations now used are within satisfactory limits.

Available hexachlorophene deodorant soaps compare favorably with ordinary toilet soaps from the point of view of pharmaceutic elegance. Apparently, hexachlorophene is compatible with cosmetically acceptable soap perfumes, dyestuffs and other constituents of soap.

On the basis of present knowledge of the physical and chemical properties of these products, certain advertising claims can be regarded as acceptable to the Committee on Cosmetics. The name deodorant soap infers that protection against offensive perspiration odor can be expected. Scientifically sound published reports offer evidence that the reduction in the numbers of resident bacteria on the skin is considerably greater than that following the use of ordinary soap, but that not all bacteria are affected by the bactericidal or bacteriostatic properties of hexachlorophene. It is also emphasized that maximum efficiency can be maintained only under certain conditions of use. That is, the hexachlorophene-containing soap must be used to the exclusion of other cleansing agents. Otherwise, the protective film of antibacterial substance will be removed in the cleansing process and the desirable effects of the cumulative action of hexachlorophene will be lost.

Until more evidence is available, it can be assumed that as long as any organisms are active on the skin, malodorous perspiration can result from their activity. Although two strains of organisms, a gram-positive bacillus and the Staphylococcus albus, are generally regarded as most responsible for disagreeable body odors, there are undoubtedly other similarly active organisms on the skin. The factor of residual bacteria after the use of these deodorant soaps also invalidates the designation "germicidal." By definition a germicide is a substance which kills all vegetative bacteria and spores in the area to which it is applied. Thus far, attempts to increase antibacterial activity by increasing the concentration of hexachlorophene in soap have been unsuccessful. In addition, the possibility of acquired resistance by the bacteria on the skin to hexachlorophene has not been thoroughly explored.

Conclusion

Deodorant soaps appear to have the potential for controlling the odor of perspiration to a degree beyond that of other types of soap. However, areas such as the axillas, the anatomic and physiologic peculiarities of which give rise to more obvious malodors, require other measures for adequate protection. The incorporation of hexachlorophene into soap does not appear to detract from the soap's pharmaceutic elegance or safety.

Council on Physical Medicine and Rehabilitation

REPORTS OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

HOWARD A. CARTER, *Secretary.*

BURDICK DIATHERMY UNIT, MODEL MF-49, ACCEPTED

Manufacturer: The Burdick Corporation, 635 Plum Street, Milton, Wis.

The Burdick Diathermy Unit, Model MF-49, is designed to produce electromagnetic oscillations centered at 27.120 megacycles (11 meter wavelength) by means of a master oscillator circuit. It is intended for use with all types of diathermy electrodes, including the "contour applicator," air-spaced electrodes, induction cable, cuff technic and instruments for minor surgery. The apparatus measures 97 by 51 by 46 cm. (38 by 20 by 18 inches); it weighs 73 Kg. (160 pounds). Packed for domestic shipping, the weight is 95 Kg. (210 pounds); for foreign shipping, it is 114 Kg. (250 pounds). Available accessories include:

Model MF-49

2 counterbalanced electrode arms
2 space-electrodes, 6¼ inches (16 cm.) in diameter, and guards
1 hinged contour applicator
1 treatment cable, 12 feet (3.6 meters)
3 cable spacers
1 cable spacer sleeve
1 cuff electrode, 4 by 13½ inches (10 by 34 cm.)
1 cuff electrode, 4 by 16 inches (10 by 41 cm.)
1 entrance cable

The unit operates on 50 or 60 cycle alternating current, and at 115 volts it draws 8.4 amperes and 560 watts. It bears the type approval number D-507 of the Federal Communications Commission.

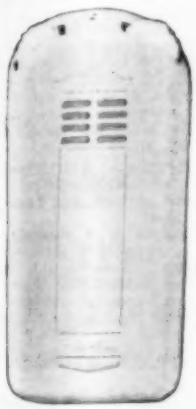
From an acceptable laboratory, the Council obtained evidence that this diathermy unit performed as represented by the manufacturer. The Council on Physical Medicine and Rehabilitation voted to include the Burdick Diathermy Unit, Model MF-49, in its list of accepted devices.

SILVERTONE HEARING AID, MODEL 103BM, ACCEPTED

Distributor: Sears, Roebuck & Company, 925 South Homan Avenue, Chicago 7.

Manufacturer: National Hearing Aid Laboratories, 815 South Hill Street, Los Angeles.

This instrument, equipped with a magnetic receiver, contains batteries, amplifier and microphone in a single metal case of conventional shape, with clothing clips at the side. The lower half of the back opens by a hinge to expose the battery compartment, which houses the two zinc-carbon batteries: the A-battery (1.5 volts) and the B-battery (22.5 volts).



Silvertone Hearing Aid Model 103BM

The outside dimensions are 130 by 61 mm. (excluding the clothing clips), with a thickness of 22 mm. above tapering to 18 mm. at the lower end. The total weight is 204 Gm.; receiver and cord together weigh 13 Gm., the batteries weigh 74 Gm. and the case alone weighs 117 Gm.

The Council obtained evidence that the physical construction of the instrument was satisfactory, that the battery drain during use was not excessive and that the device gave adequate acoustic gain in clinical tests. The Council on Physical Medicine and Rehabilitation voted to include the Silvertone Hearing Aid, Model 103BM, in its list of accepted devices.

SONOTONE HEARING AIDS, MODELS 910 AND 920, ACCEPTED

Manufacturer: Sonotone Corporation, Box 112, Elmsford, N. Y.

These two Sonotone electronic hearing aids are conventional in shape and appearance. Model 910 is designed for small size and light weight, while Model 920 is designed to operate for longer periods without the changing of batteries. The dimensions and weights are as follows:

	Model 910	Model 920
Thickness	19 mm.	19 mm.
Width	57 mm.	57 mm.
Length	92 mm.	108 mm.
Weight	120 Gm.	142 Gm.
Shipping weight, avoirdupois	15 oz.	24 oz.
Shipping weight, metric	425 Gm.	680 Gm.

Both models are designed to run on zinc-carbon dry cells, the A-battery at 1.5 volts and the B-battery at 22.5 volts. Model 910 can be fitted with a battery cord and connectors for the use of an external A-battery.

Sonotone Hearing Aid, Model 910

The manufacturer also submitted bone-conduction "oscillators" bearing the identification symbols "01" and "02," accompanied with spring headbands and air-conduction receivers identified as "U-1" (one dot) and "U-2" (two dots). Physical and clinical tests showed that both instruments and their accessories were well designed and satisfactory with respect to acoustic gain, discrimination, tone quality, clothing noise and inherent electrical noise.

The Council on Physical Medicine and Rehabilitation voted to include the Sonotone Hearing Aid, models 910 and 920, in its list of accepted devices.

CARBATOM ATOMIZER ACCEPTED

Manufacturer: The York Precision Company, Inc., Perry and Thomas Avenues, York, Pa.

The Carbatom Atomizer is a sprayer or insufflator energized by compressed carbon dioxide from cartridges. The latter are supplied by the manufacturer of the device but are also available at drug stores. The device is designed primarily for the administration of aqueous and alcoholic solutions, but it is also capable of spraying oily solutions and even creams.

The Carbatom

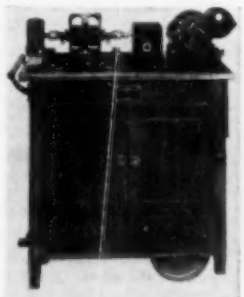
The apparatus proper weighs about 0.5 Kg. (1 pound) and consists of a central arrangement of metal tubes and passages that connect with a nozzle, a handle, a cartridge of carbon dioxide and a metal cylinder in which the carbon dioxide encounters the liquid that is to be sprayed. The cylinder must be strong enough to withstand pressures of the same order of magnitude as those inside the cartridge. Packed with accessories for shipment, the assembly weighs 4.3 Kg. (9½ pounds).

Evidence obtained from a source acceptable to the Council indicated that the apparatus was well constructed and easy to handle, and that it gave a strong, steady spray of solutions placed in the spray bottle. The Council on Physical Medicine and Rehabilitation voted to include the Carbatom Atomizer in its list of accepted devices.

CAMBRIDGE ALL-ELECTRIC MOBILE ELECTROCARDIOGRAPH ACCEPTED

Manufacturer: Cambridge Instrument Company, Inc., Grand Central Terminal, New York 17, N. Y.

The Cambridge All-Electric Mobile Electrocardiograph employs a string galvanometer and is equipped for photographic recording. It operates on a 110 volt, 60 cycle alternating current or (if specified) on a 110 volt direct current, no batteries being used. The photographic recorder uses either film or paper 6 cm. wide in rolls 53 meters (175 feet) in length. It records at speeds of 25 or 50 mm. per second.



Cambridge All-Electric Mobile Electrocardiograph

The cabinet is fitted with two rubber-tired wheels and a swivel caster which make it freely movable. The over-all dimensions are 107 by 53 by 99 cm. (42 by 21 by 39 inches), and the total weight is 131 Kg. (291 pounds). The shipping weight is 211 Kg. (465 pounds). Accessories include four direct-contact electrodes, one exploring chest electrode, one roll of photographic paper and a tube of Cambridge electrode jelly.

On the basis of satisfactory electrophysical and clinical evidence the Council on Physical Medicine and Rehabilitation has voted to include the Cambridge All-Electric Mobile Electrocardiograph in its list of accepted devices.

SAFE-T-RING PROPHYLACTICS ACCEPTED

Manufacturer: National Prophylactics Company, Inc., 123 East 24th Street, New York 10.

The Safe-T-Ring Prophylactic is a condom, or rubber sheath, that is distinguished from the usual condom by a rubber band or ring that is attached near the open (proximal) end.

The Council obtained satisfactory evidence that this device fulfils the Council's requirements for acceptance of contraceptive devices. The Council on Physical Medicine and Rehabilitation voted to include the Safe-T-Ring Prophylactic in its list of accepted devices.

Council on Pharmacy and Chemistry

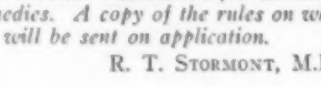
NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

HYDROXYAMPHETAMINE HYDROBROMIDE.—

Paredrine Hydrobromide.—(SMITH, KLINE & FRENCH).—*para*-(2-Aminopropyl)phenol hydrobromide.—1-(*p*-Hydroxyphenyl)-2-aminopropane hydrobromide.—$C_9H_{13}BrNO$.—M.W. 232.13.—The structural formula for hydroxyamphetamine hydrobromide may be represented as follows:



Actions and Uses.—Hydroxyamphetamine hydrobromide shares the general properties of other sympathomimetic amines. Animal studies indicate it to be somewhat less toxic than epinephrine and amphetamine. It produces little or no ephedrine-like central stimulation. Its principal therapeutic usefulness is therefore dependent on its peripheral effects. It is employed in solution as the hydrobromide for topical application to produce shrinkage of the nasal mucosa. For this purpose, at equal dosage levels, it is considered to be about twice as effective as ephedrine, in terms both of quickness and duration of action, and also less irritating. Solutions of the drug instilled in the eye produce mydriasis but little cycloplegia, so that it is not recommended for ophthalmic use. By injection or by oral administration, the drug produces cardiovascular and intestinal effects similar, though not identical, to other sympathomimetic agents, but its systemic actions are not considered sufficiently outstanding to warrant such use of the drug.

Dosage.—Hydroxyamphetamine hydrobromide is used in 1 per cent solution for topical application by instillation, tamponage or by atomized spray into the nostrils for shrinking of the nasal mucosa. The administration of 2 to 5 drops four to five times daily is usually sufficient for instillation. For sinus irrigation or displacement, the 1 per cent solution should be diluted with three parts of isotonic sodium chloride solution to make a 0.25 per cent solution of the drug.

Tests and Standards.—

Hydroxyamphetamine hydrobromide occurs as a white, crystalline solid having a faint odor. It melts between 189 and 192 C. It is very soluble in water, freely soluble in alcohol and practically insoluble in benzene and ether. A 2 per cent aqueous solution of hydroxyamphetamine hydrobromide has a *p*H between 4.5 and 5.5. Saturate a 10 per cent solution of the hydrobromide with potassium carbonate, extract with ether and remove the ether by evaporation. The organic base thus obtained occurs as a white to faintly yellow crystalline solid, melting between 127 and 129 C. It is soluble in acids and strong alkalis.

Dissolve about 2 Gm. of ammonium molybdate in 20 ml. of sulfuric acid. To 20 ml. of this solution add about 10 mg. of hydroxyamphetamine hydrobromide: an emerald-blue color develops *(distinction from amphetamine, ephedrine, methamphetamine, naphazoline, Nethamine, phenylpropanolamine, phenylpropylmethylamine and Tuamine).* Dissolve about 10 mg. of hydroxyamphetamine hydrobromide in 10 ml. of water. Add 0.5 ml. of ferric chloride T. S.: a purple color develops *(distinction from epinephrine and 1-(3',4'-dihydroxyphenyl)-2-isopropylaminoethanol, which give a green color).* Dissolve about 10 mg. of hydroxyamphetamine hydrobromide in 10 ml. of diluted hydrochloric acid. Cool in an ice-salt bath and add 5 ml. of 20 per cent sodium nitrite solution. Shake and allow to stand for about 5 minutes in the ice-salt bath. Add 10 ml. of chloroform and shake. The chloroform layer is amber in color *(distinction from phenylephrine and Synephrine, which impart a blue color to the chloroform layer).* Dissolve about 10 mg. of hydroxyamphetamine hydrobromide in 2 ml. of water. Acidify with 1 ml. of diluted nitric acid and add 1 ml. of silver nitrate T. S.: a pale yellow precipitate is produced which is slightly soluble in ammonia T. S. *(bromide).*

Dry about 1 Gm. of hydroxyamphetamine hydrobromide, accurately weighed, at 110 C. for 3 hours: the loss in weight does not exceed 0.5 per cent.

Char about 2 Gm. of hydroxyamphetamine hydrobromide, accurately weighed, over a low flame. Cool, then add 1 ml. of sulfuric acid and continue ignition until no carbon remains: the residue should not exceed 0.1 per cent on a dry weight basis.

Transfer 0.15 Gm. of hydroxyamphetamine hydrobromide, accurately weighed, to a 100 ml. volumetric flask and dilute to the mark with alcohol. Mix thoroughly and transfer 10 ml. of the solution to another 100 ml. volumetric flask. Dilute to 100 ml. with alcohol, mix well and transfer 10 ml. of the solution to a third 100 ml. volumetric flask and dilute to the mark. The final solution (0.0015 per cent) exhibits ultraviolet absorption maxima at 2550 A ($E^{1\%}_{cm.} = 370 \pm 5$) and 2780 A with a minimum at about 2440 A. The ration of the observed optical densities at 2250 A and 2780 A should be between 4.3 and 5.4.

Transfer about 0.5 Gm. of hydroxyamphetamine hydrobromide, accurately weighed, to a 100 ml. volumetric flask. Add 50 ml. of distilled water and 3 ml. of nitric acid. Mix thoroughly, add exactly 25 ml. of 0.1 *N* silver nitrate and fill to the mark with distilled water. Shake the mixture vigorously and allow the silver bromide to settle out. Transfer exactly 50 ml. of the clear supernatant solution into a flask and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate, using ferric ammonium sulfate T. S. as an indicator. Each ml. of 0.1 *N* silver nitrate is equivalent to 0.008092 Gm. of hydrogen bromide: the amount of hydrogen bromide is not less than 34.0 nor more than 35.2 per cent.

Transfer 0.2 Gm. of hydroxyamphetamine hydrobromide, accurately weighed, to a separatory funnel, add 20 ml. of water and 25 ml. of ether and shake the mixture. Add 15 Gm. of reagent quality potassium carbonate and agitate immediatly. After the potassium carbonate is completely dissolved, shake the solution for about 1 minute and separate the ether layer. Continue the extraction with six additional 25 ml. portions of ether. Combine the ether extracts and filter through an ether-wetted filter paper into a 250 ml. Erlenmeyer flask containing 20 ml. of 0.1 *N* sulfuric acid. Remove the ether by evaporation on a steam bath and titrate the excess acid with 0.1 *N* sodium hydroxide using methyl red T. S. as an indicator. Each ml. of 0.1 *N* sulfuric acid is equivalent to 0.02321 Gm. of hydroxyamphetamine hydrobromide: the amount of hydroxyamphetamine hydrobromide is not less than 97.5 nor more than 101.0 per cent.

HYDROXYAMPHETAMINE HYDROBROMIDE SOLUTION: Add several drops of the aqueous hydroxyamphetamine hydrobromide solution to 2 ml. of a solution containing 1 Gm. of ammonium molybdate in 10 ml. of concentrated sulfuric acid: a blue color develops.

Transfer exactly 20 ml. of the aqueous solution to a separatory funnel, add 25 ml. of ether, 15 Gm. of reagent quality potassium carbonate and agitate until the solid has dissolved. Proceed with the assay as described in the monograph on Hydroxyamphetamine Hydrobromide beginning with "After the potassium carbonate is completely dissolved. . . ." The amount of hydroxyamphetamine hydrobromide is not less than 95.0 nor more than 105.0 per cent.

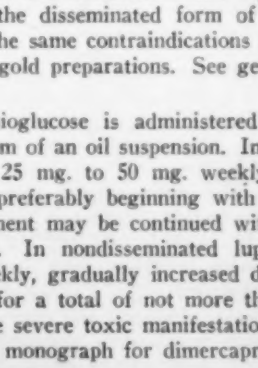
SMITH, KLINE & FRENCH LABORATORIES, PHILADELPHIA 5.

Aqueous Solution Paredrine Hydrobromide: 30 cc. and 360 cc. bottles. An aqueous solution containing 10 mg. of hydroxyamphetamine hydrochloride in each cc. Preserved with sodium ethylmercurithiosalicylate 1:100,000.

U. S. patent 2,181,845; U. S. trademark 334,351.

AUROTHIOGLUCOSE.—Solganal (SCHERING).—

$C_6H_{11}AuO_5S$.—M.W. 392.41.—The structural formula of aurothioglucose may be represented as follows:



Actions and Uses.—Aurothioglucose shares the same therapeutic purposes and toxic manifestations of other organic nonionizing gold compounds; it is used for the treatment of active rheumatoid arthritis and nondisseminated lupus erythematosus. It is harmful in the disseminated form of the latter disease and is subject to the same contraindications and precautions as for other injected gold preparations. See general statement on gold compounds.

Dosage.—Aurothioglucose is administered by intramuscular injection in the form of an oil suspension. In active rheumatoid arthritis doses of 25 mg. to 50 mg. weekly are given for a total of 1.0 Gm., preferably beginning with a dose of 10 mg. If tolerated, treatment may be continued with longer intervals between injections. In nondisseminated lupus erythematosus, biweekly, then weekly, gradually increased doses of 0.1 mg. to 50 mg. are given for a total of not more than 1.0 to 1.5 Gm.

Treatment of the severe toxic manifestations of gold therapy is discussed in the monograph for dimercaprol.

Tests and Standards.—

Physical Properties: Aurothioglucose occurs as a yellow to yellow-green powder. It is almost odorless and tasteless. It is soluble in water, but decomposes on standing. It is insoluble in acetone, alcohol, chloroform and ether.

Identity Test: The procedures described for the determination of gold and sulfur under "Assay" serve as identity tests.

Accurately weigh approximately 0.1 Gm. of previously dried aurothioglucose. Transfer it to a 10 ml. volumetric flask, fill to the mark with distilled water and determine the optical rotation using a 100 mm. tube. The specific rotation, $[\alpha]_D^{25}$, is between +65 and +73°.

Purity Tests: Dry about 1 Gm. of aurothioglucose, accurately weighed, in a vacuum desiccator over phosphorus pentoxide for 24 hours: the loss in weight does not exceed 1 per cent.

Assay: Accurately weigh approximately 0.5 Gm. of dried aurothioglucose. Transfer it to a 250 ml. beaker and dissolve in 100 ml. of distilled water. Add 10 ml. of concentrated nitric acid: the solution becomes dark brown to black. Heat the solution to boiling and boil for 5 minutes. Filter the solution through ashless filter paper into a 500 ml. beaker and wash thoroughly with distilled water. Preserve the filtrate for the sulfur determination. Transfer the gold residue and filter paper to a tared silica crucible and ignite to constant weight. The sample contains not less than 49.4 nor more than 51.0 per cent gold.

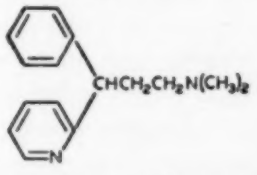
Evaporate the filtrate from the gold determination to about 15 ml., add 15 ml. of hydrochloric acid and boil for about 5 minutes to remove oxides of nitrogen. Add about 400 ml. of distilled water and again bring the solution to boiling. Add dropwise, with constant stirring, 10 ml. of barium chloride T. S. Allow the solution to stand overnight. Transfer the precipitate to a tared Gooch crucible and wash with distilled water. Dry the crucible in an oven at 105° C. for 15 minutes then place it inside a larger crucible and ignite with a full flame to constant weight. Each Gm. of barium sulfate corresponds to 0.1373 Gm. of sulfur: the amount of sulfur is not les than 8.0 nor more than 8.4 per cent.

SCHERING CORPORATION, BLOOMFIELD, N. J.

Suspension Solganal in Oil: 1.5 cc. ampuls: A suspension in sesame oil containing 6.7 mg., 16.7 mg. and 33.3 mg. of aurothioglucose in each cc.; 10 cc. vials. A suspension in sesame oil containing 10 mg., 50 mg. and 100 mg. of aurothioglucose in each cc. Preserved with 0.1 per cent propylparaben.

U. S. trademark 261,372.

PROPHENPYRIDAMINE. — Trimeton (SCHERING).— 1-Phenyl-1-(2-pyridyl)-3-dimethylaminopropane.—$C_{16}H_{20}N_2$.— M.W. 240.34.—The structural formula for prophenpyridamine may be represented as follows:



Actions and Uses. — See general statement on Histamine-Antagonizing Agents. Sedation and gastrointestinal irritation are common with prophenpyridamine.

Dosage.—The average adult dose is 25 to 50 mg.

Tests and Standards.—

Physical Properties: Prophenpyridamine occurs as an oily liquid with a slightly yellow color and an amine-like odor. Its index of refraction is between 1.5519 and 1.5521, and its specific gravity is about 1.0081. The liquid boils around 135 C. at 0.5 mm. and 181 C. at 13 mm. It is insoluble in water, but soluble in alcohol, benzene, chloroform, ether and in dilute acids.

Identity Tests: Add 2 drops of prophenpyridamine in 2 ml. of alcohol and then add 5 drops of chloroform and 0.5 ml. of 50 per cent potassium hydroxide. On heating, a red color develops, but no odor of isonitriles is obtained (*absence of primary amine*).

Add about 0.5 Gm. of prophenpyridamine to a saturated alcoholic solution of picric acid at 65 C. Allow the reaction mixture to digest at this temperature for about 20 minutes. The yellow crystalline dipicrate melts between 198 and 204 C.

Assay: (Prophenpyridamine) Transfer about 0.3 Gm. of prophenpyridamine, accurately weighed, to a 100 ml. volumetric flask and dilute to the mark with alcohol. Mix thoroughly and transfer 10 ml. of the solution to another 100 ml. volumetric flask. Dilute to 100 ml. with alcohol, mix well and transfer 10 ml. of the solution to a third 100 ml. volumetric flask and dilute to 100 ml. The final solution (0.003 per cent) exhibits an ultraviolet absorption maximum at 2630 A ($E_{cm.}^{1\%} = 184 \pm 3$), a sharp inflection in the curve at about 2690 A and a minimum at about 2380 A.

Transfer 0.25 Gm. of prophenpyridamine accurately weighed, to a 150 ml. beaker and dissolve in 50 ml. of a 1:1 alcohol-water solution. Run a potentiometric titration with 0.1 *N* hydrochloric acid using a glass electrode. Each ml. of 0.1 *N* hydrochloric acid is equivalent to 0.02403 Gm. of prophenpyridamine. The amount of prophenpyridamine present is not less than 98.5 nor more than 100.5 per cent.

(Nitrogen) Transfer about 0.15 Gm. of prophenpyridamine, accurately weighed, to a semi-micro Kjeldahl flask and digest for 3 hours with 7 ml. of sulfuric acid, 2.7 Gm. of potassium sulfate and 0.3 Gm. of mercuric oxide. Dilute the clear solution to 15 ml. with water, make it alkaline with 40 per cent sodium hydroxide and then add 10 ml. of 40 per cent sodium thiosulfate. Distil the ammonia into 20 ml. of 4 per cent boric acid. Using a mixed indicator (1 part of methyl red T.S.: 5 parts of bromocresol green T.S.), titrate the liberated ammonia with 0.05 *N* sulfuric acid. Each ml. of 0.05 *N* sulfuric acid is equivalent to 0.0007004 Gm. of nitrogen. The amount of nitrogen present is not less than 11.50 nor more than 11.80 per cent.

PROPHENPYRIDAMINE TABLETS:

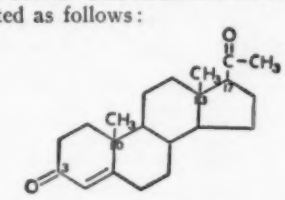
Identity Tests: Crush 10 tablets and extract the powdered material with ether. Filter the ether extract and evaporate the solvent. To the residue add a saturated alcoholic solution of picric acid at 65 C. Digest for 20 minutes at 65 C. and remove the solid dipicrate by filtration. The yellow crystals melt between 198 and 204 C.

Assay: Powder about 20 tablets and transfer the equivalent of 0.25 Gm. of prophenpyridamine to a Soxhlet extractor and extract with 75 ml. of ether for 6 hours. Remove the ether by evaporation and dissolve the residue in 50 ml. of 1:1 alcohol-water solution. Run a potentiometric titration with 0.1 *N* hydrochloric acid using a glass electrode. Each ml. of 0.1 *N* hydrochloric acid is equivalent to 0.02403 Gm. of prophenpyridamine. The amount of prohenpyridamine present is not less than 95 nor more than 105 per cent of the labeled amount.

SCHERING CORPORATION, BLOOMFIELD, N. J.

Tablets Trimeton: 25 mg.

PROGESTERONE-U. S. P. — 4-Pregnene-3,20-dione.— $C_{21}H_{30}O_2$.—M.W. 314.45. The structural formula of progesterone may be represented as follows:



For description and standards see the U. S. Pharmacopeia under Progesterone and Progesterone Injection.

Actions and Uses.—Progesterone, a synthetic crystalline hormone principle of the corpus luteum, is of value in the treatment of functional uterine bleeding ("metropathia hemorrhagica"). Its use for the treatment of primary or secondary amenorrhea, with or without estrogen, is still experimental. Although it has long been employed in the treatment of threatened or habitual abortion, dysmenorrhea, menorrhagia, etc., satisfactory evidence is insufficient to establish its effectiveness for these conditions.

Dosage.—Progesterone is ineffective orally. It is administered either intramuscularly in oil solution in doses up to 20 mg. daily or subcutaneously in aqueous suspension in doses of 5 to 10 mg. daily. The aqueous suspension is four times as active as the oil solution, so that in the latter form, larger doses of the oil solution are required to produce effects equivalent to those obtained with smaller doses of the aqueous suspension. This difference is only quantitative.

LINCOLN LABORATORIES, INC., DECATUR, ILL.

Aqueous Suspension Progesterone: 10 cc. vials: A suspension containing 10 mg. (10 I.U.) of progesterone in each cc. of physiological isotonic sodium chloride solution. Preserved with 0.5 per cent phenol.

PENICILLIN FOR PARENTERAL USE FOR PROLONGED ACTION (See New and Nonofficial Remedies 1949, p. 153).

The following dosage form has been accepted.

MERCK & COMPANY, INC., RAHWAY, N. J.

Crystalline Procaine Penicillin G in Oil: Bulk and 10 cc. vials: 300,000 units in each cc. in peanut oil with 2 per cent aluminum monostearate.

TESTOSTERONE PROPIONATE-U. S. P. (See New and Nonofficial Remedies 1949, p. 407).

The following dosage form has been accepted:

TESTAGAR & CO., INC., DETROIT 26.

Solution Testosterone Propionate in Oil: 10 cc. and 30 cc. vials: A solution in peanut oil containing 25 mg. of testosterone propionate in each cc. 10 cc. vials: A solution in peanut oil containing 50 mg. of testosterone propionate in each cc. Preserved with 0.5 per cent of chlorobutanol.

***d*-TUBOCURARINE CHLORIDE** (See New and Nonofficial Remedies 1949, p. 210).

The following dosage forms have been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Solution *d*-Tubocurarine Chloride: 20 cc. vials: A solution containing 3 mg. of *d*-tubocurarine chloride in each cc.

Solution *d*-Tubocurarine Chloride (High Potency): 1 cc. ampuls: A solution containing 15 mg. of *d*-tubocurarine chloride in each cc.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET · · CHICAGO 10, ILL.

Edited by
AUSTIN SMITH, M.D.

Associate Editor
JOHNSON F. HAMMOND, M.D.

Editor for Current Medical Literature, GEORGE HALPERIN, M.D.

Subscription price · · Twelve dollars per annum in advance

Cable Address · · · "Medic, Chicago"

Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter

SATURDAY, MARCH 18, 1950

"MISSION ACCOMPLISHED: THE TASK AHEAD"

In his presidential address before the American Surgical Association, Dr. Fred W. Rankin [1] presented an extensive review of the immediate care and rehabilitation of battle casualties in World War II. Since he served in both World Wars and was chief of the Surgical Consultants Division of the Surgeon General's Office in the recent war, Dr. Rankin was in an excellent position to observe the development of the surgical program. Within a few weeks after this country declared war a professional services division was established. The consultants served continuously and in uniform, on the concept that medicine should be practiced on a parallel to that in civilian life, namely, by specialization. In World War I the consultants division consisted of a casual group of medical men serving only part time, and many of them were not in uniform. The consultant system was the keystone of the arch of the laudable record achieved in World War II. Its full implementation, however, was attended with organizational difficulties, some of which were caused by bulk allotment of personnel, a rigidity of unit organization, limitations of rank and the absence of a consultant specification in Tables of Organization. Nevertheless, the consultants refused to be shackled, and their forceful personalities overcame the limitations of authority and the subordination of the Medical Corps to a Service of Supply which dealt in commodities and in nonprofessional services.

The medical personnel of the Fifth Army in the Mediterranean theater of operations, Rankin said, was probably the best ever supplied to an army operating in the field. In the European theater the care of the wounded was admirably accomplished, owing largely to the indomitable spirit and remarkable personality of the late Gen. Elliott C. Cutler. In the Pacific theater the consultant system came into being late and was never fully implemented partly because of the shortage of personnel and of the deliberate postponement of the major effort in that area until the European phase of the war was concluded. The greatest achievement of the consultants in the Zone of the Interior was the establishment in the general hospitals of specialized surgical centers—six amputation centers, twenty-one neurosurgical centers, five thoracic surgery centers, three vascular surgery centers, eight plastic surgery centers, eight ophthalmologic surgery centers, two centers for rehabilitation of the blind and three for rehabilitation of the deaf, all of which were staffed by highly competent men.

The percentage of men dying of wounds in World War II was 3.3, as compared with 8.1 in World War I. The mortality rates in World War II for wounds of the head, chest and abdomen were almost 65 per cent lower than those for World War I. The factors which vitally influenced the mortality and morbidity rates for battle injuries in the last World War were the availability of a large number of excellently trained young surgeons for service forward in combat areas, improved methods of resuscitation, including among others the lavish use of blood and blood plasma, the control of infections by antibiotics and chemotherapeutic agents as adjuncts to surgery and improved transportation facilities, particularly transportation by air.

The three stages of wound management, (1) early and complete débridement, (2) delayed wound closure and (3) reconstructive surgery, were exactly like the principles employed in World War I; but they were modified and refined in practice with infinite advantage to the wounded soldier. Débridement was done close to the front line; transportation facilities permitted rapid evacuation to hospitals far to the rear for the second phase of the program, and nearly all the reconstructive surgery was done in hospitals in the Zone of the Interior. The properly conducted second stage of wound management in the base area, following a properly conducted débridement in the forward area, was at the heart of the satisfactory mortality and morbidity statistics of this war.

Wounds of the extremities approximated 83 per cent of all battle-incurred wounds. Although exact figures were not available, Rankin expressed his belief that the fractures incurred in training, maneuvers and similar activities equaled or perhaps exceeded the number incurred by enemy action. In World War II there was remarkable improvement in the technical phases of management of compound fractures in forward hospitals and in the broad application of such procedures as early secondary closure or delayed internal fixation of malalined compound fractures in base hospitals. The surgical program of management of compound fractures in their early stages was based on: excision of dead tissue; obliteration of dead space or its depen-

1. Rankin, F. W.: Mission Accomplished: The Task Ahead, Ann. Surg. 1: 289 (Sept.) 1949.

dent drainage; staged closure of the wound; atraumatic technic, with fine hemostats and ligatures; pressure dressings; adequate reduction and immobilization; precise splinting, and the adjuvant use of penicillin and whole blood.

Nerve injuries constituted nearly 10 per cent of all battle casualties and in seriousness and duration of necessary treatment were second only to the orthopedic load. Although the management of acute penetrating wounds of the brain followed without essential modification the basic concepts formulated by Harvey Cushing in World War I, the neurosurgeon in World War II had almost perfect control of infections which often turned success to failure in the earlier war. A most important lesson about head trauma learned in World War I and proved again in World War II was that it was not necessary to hurry an emergency operation unless the patient's condition was deteriorating. The patient was, in fact, better for a delay which permitted adequate resuscitation and also operation later under optimum conditions. A significant contribution by Army neurosurgeons was the establishment in the Surgeon General's Office of a peripheral nerve registry in which thousands of peripheral nerve injuries were entered and from which, when the final analysis has been completed at the close of the appointed five year period, the results of peripheral nerve surgery in World War II will be clear. Thus the pattern will be established for the proper management of similar civilian injuries. The transportation of casualties with spinal cord injuries was an achievement in itself. These casualties were evacuated as soon as possible to one of the twenty-one paraplegic centers in the Zone of the Interior, where a rehabilitation program was begun. Much credit for the success of this program belongs to the urologists, orthopedic physicians, rehabilitation and dietary experts, physical therapists and other specialists, who shared responsibility with the neurosurgeons and all of whom provided an example of wholehearted, efficient cooperation that is unique in Army and civilian practice alike. The goal of the Army paraplegic program, to enable every such casualty to resume his former place in civilian life, has been achieved far beyond what was expected.

An astonishingly low mortality was achieved in the centers for the specialized care of vascular injuries located at Ashford General Hospital, Mayo General Hospital and DeWitt General Hospital. Only four deaths occurred in these centers in 803 operations for aneurysm and arteriovenous fistula. The functional results of these operations were equally remarkable. Patients with cold injuries, chiefly trench foot, also were treated at these centers with a brilliant record, which counterbalances in part the record of failure to prevent trench foot, which, Rankin said, is one of the blots on the Army record in World War II and one which would have been quite different if the warnings of the Surgical Consultants Division had been heeded by command.

The mortality from abdominal wounds was reduced to between 25 and 35 per cent from between 60 and 75 per cent in World War I. Although no outstanding changes in technic were developed, it became routine in World War II to exteriorize all wounds of the colon, except those of the cecum and ascending colon, which could be handled, like wounds of the small intestine, by primary suture. It also became routine to perform colostomy in all wounds of the rectum. Early in the war sulfonamide compounds were introduced into the peritoneal cavity in all abdominal wounds, but this method was abandoned later because of the danger of adhesions and intestinal obstruction. Wounds of the liver were rapidly fatal in a high proportion of cases. Enormous damage was done to the parenchyma of the liver, especially when the missile had been fired at short range. Nevertheless a surprising number of lives was saved by immediate operation on wounds of the liver.

The final statistics on injuries of the chest are still to be compiled. Rankin was of the opinion, however, that they will be lower than in any previous war. The availability of chemotherapeutic and antibiotic agents and of large supplies of blood and refinements in surgical technic had much to do with increasing these survival rates. More important were the judicious timing and proper selection of surgical procedures and adequate resuscitative measures. Patients were not operated on until shock was controlled and their condition stabilized. A rapidly fatal outcome could be expected if accumulations of blood and mucus in the trachea or bronchi were not promptly removed by catheter suction or bronchoscopy. The control of pain originating in the chest wall from injuries by injections of procaine at the site of the injury and by paravertebral block were important in the management of shock in thoracic wounds. A lesson learned in this war was prompt evacuation of the hemothorax, without air replacement, in battle-incurred thoracic injuries. Failure to do so was likely to be followed by chronic hemothorax or fibrothorax and later by secondary infection. Army hospitals today are not filled with respiratory cripples as they were for years after World War I, in many instances because of empyema which followed the ultraconservative treatment of traumatic hemothorax. Chronic empyema, in fact, was actually rare in World War II. The ultimate objective in the management of hemothorax was early, complete reexpansion of the lung, with conservation of as much cardiopulmonary function as possible, and this was achieved in a remarkable number of cases. Favorable results were achieved in a large number of cases of bronchiectasis, most of which

were not related to chest wounds and many of which were successfully treated by surgical extirpation of the diseased lung tissue.

Rankin paid tribute also to the plastic surgeons, who performed some 40,000 operations in World War II without a death. At one time 33,000 operations were scheduled for performance on the 11,000 patients then in the plastic surgery centers. Many of the plastic surgeons had to be kept in the Army for a year or more longer than their associates because the work they were doing could be done by no one else. Plastic surgeons may be proud of their devotion to the reconstruction of wounded young soldiers who seemingly had been marred for life. Rankin requested his advisor in plastic surgery in the Surgeon General's Office to outline the highlights of plastic surgery as practiced in World War II. The following points were listed:

1. The elimination of tannic acid in the management of burns and the substitution of atraumatic care of the wound, the use of pressure dressings to prevent loss of serum and early skin grafting.

2. The early closure of wounds, either by grafting or by suture, with or without the utilization of flaps.

3. The establishment of specialized centers and of specialized teams in the combat zone for the immediate care of casualties suffering from burns and facial injuries. The superior functioning of these services cut down materially the time required for the definitive and long-drawn-out plastic repairs to be done in the Zone of the Interior.

4. The extensive use of local tissue in repairs.

5. The fundamental principle of wound closure, which was highly developed by plastic surgeons and which was used in many cases preliminary to secondary orthopedic or neurosurgical procedures on the deeper tissues.

6. The concept that deep healing can be no better than superficial healing.

7. The close cooperation of plastic surgeons with dentists, anesthestists, orthopedic surgeons, neurosurgeons and the nursing service in the management of their casualties.

8. Special procedures devised for the management of injuries in particular regions, including the palate, the jaw, the nose, the ear and other parts of the face, the lower extremities and the hands.

Looking to the future, Rankin said that the introduction of atomic weapons may possibly change the entire concept of the surgery of trauma and, indeed, may change the entire plan of medical practice. It will call for an entirely different type of cooperation between military and civilian authorities. Such possibilities demand realistic thinking, courageous, unselfish patriotism and a high order of statesmanship. The uncertain future should make us hasten to digest the lessons of the last war and to integrate civilian and medicomilitary agencies. It is essential that the medical profession coordinate its efforts and assume leadership for an over-all plan in order to avoid the almost complete absence of medical plans that characterized World War II. Civilian agencies, he said, should dominate the direction of all efforts at the beginning, should another conflict occur.

UNAUTHORIZED REFERENCES TO MEDICAL JOURNALS

From time to time reference is made in advertising broadsides to an article in a medical journal to lead the reader of the promotional literature into believing that the advertised product has the endorsement of the journal. The American Medical Association receives inquiries about these implied endorsements, and it is found in many cases that the references are used without permission from the journals cited in the advertisements. When references are designed to attract the attention of qualified readers and consist of factual unbiased presentations they can serve a useful purpose. Often, however, the complaints received at A. M. A. headquarters concern advertisements for products whose usefulness is questionable, firms whose integrity is in doubt or products that are promoted for sale to the laity.

The public today generally is aware of the many remarkable medical advances, and it is susceptible to the glowing terms with which copy writers describe each "miracle" drug or device. The prospective user naturally hopes that something will cure his ailments, even when these exist only in his imagination. In fact, he has come to expect miracles because of the ceaseless bombardment he receives from news items, advertising splurges and radio announcements. Those who are responsible for the deceptive practices may resort to half truths or complete falsification. They are oblivious to moral obligations in deference to selfish interests, but they cannot escape their responsibility simply by saying "I can't help what the other person wants to believe." If a product cannot be sold without untruthful or misleading statements it probably is not worthy of much attention by anyone.

When reference is found to advertisements in publications of the American Medical Association observers are free to ask for information. Advertising which conforms to the rules of the councils is supervised constantly. The advertising rules of the American Medical Association declare in part: "Advertisements will not be accepted which, either by intent or inference, would result in deceiving, defrauding or misleading the reader. . . . If testimonials or quotations appear in advertising the validity of the claims made and the probable import on the reader will be subject to critical appraisal before acceptance. . . . Quotation or excerpts from published papers are not accepted if by themselves they distort the true meaning intended by the authors or are otherwise misleading. Quotations from the Association's publications may be used in advertisements only with express permission in each instance." Each issue of THE JOURNAL OF THE AMERICAN MEDI-

CAL ASSOCIATION carries this statement: "Matter appearing in all publications of the American Medical Association is covered by copyright. Permission will be granted on request for reproduction in reputable publications if proper credit is given. Reproduction for commercial purposes will not be permitted."

THE JOURNAL intends to take such steps as are necessary to enforce these policies in the interest of its readers and of the public.

Current Comment

EFFECTS OF PLACEBOS

A recent report by Stewart Wolf [1] reemphasizes that placebos may produce observable effects which must be remembered when drug medication is instituted. When a drug is applied to an isolated tissue suspended in a standard solution the response usually is predictable and reproducible. This is not necessarily true, however, for intact tissue; modifying factors may influence profoundly the tissue reaction. Using urogastrone, diphenhydramine hydrochloride, sterile water, ipecac, neostigmine, tap water, lactose and atropine on a patient with a large gastric fistula, through which the gastric mucous membrane could be observed, and 4 other human subjects for supplementary experimental work, Wolf observed "placebo effects" which can modify the actions of drugs; in fact, the "placebo effects" may surpass the actions attributable to the drugs. He contends that these are not imaginary but may be associated with measurable changes at the end organs. He warns again of the difficulty of evaluating new remedies in patients and urges curbing of enthusiasm until one has accounted for the physiologic effects of the "placebo" action.

FLOTATION OF CANCER CELLS

In 1946-1947 Ferrebee [1] and Vallee and others [2] reported the successful separation of leukocytes from erythrocytes by flotations on isosmotic bovine serum albumin solutions. The separation was made possible by the relatively low specific densities of leukocytes. The specific density of human erythrocytes is about 1.09; that of human leukocytes varies from 1.07 to 1.08. Fawcett and associates [3] of the Department of Anatomy, Harvard University, and the Department of Biology, Massachusetts Institute of Technology, applied the same technic to the separation of malignant cells from pleural and abdominal fluids of cancer patients. The original serosanguinous fluids were centrifuged and the resulting clear supernatant fluids decanted. The residues were suspended in one-tenth the original volume of isotonic saline solution. Five cubic centimeters of the resuspended material then were carefully placed as a layer over 5 cc. of bovine albumin solution. The specific density of the selected albumin dilution varied from 1.05 to 1.06. The tubes containing the resuspended material and bovine albumin were centrifuged for five minutes at 500 revolutions per minute, then for thirty minutes at 3,000 revolutions per minute. At the end of this period the erythrocytes, leukocytes and cellular debris were at the bottom of the bovine albumin solution as a sediment, while the malignant cells were concentrated in a thin layer above the albumin solution. A few normal mesothelial cells were usually found in the malignant layer. This demonstration of the low specific density of cancer cells provides a simple means of obtaining relatively pure populations of neoplastic cells for chemical and physical investigation. The flotation method presumably may be applied to the concentration of desquamated malignant cells in vaginal fluids.

1. Wolf, S.: Effects of Suggestion and Conditioning on the Action of Chemical Agents in Human Subjects: The Pharmacology of Placebos, J. Clin. Investigation **29**: 100 (Jan.) 1950.

1. Ferrebee, J. W., and Geiman, Q. M.: J. Infect. Dis. **78**: 173, 1946.

2. Vallee, B. L.; Hughes, W. L., Jr., and Gibson, J. G., II: Blood, 1947, special issue no. 1, p. 82.

3. Fawcett, D. W.; Vallee, B. L., and Soule, M. H.: Science **3**: 34 (Jan. 13) 1950.

SEX CRIMES

Civic-minded persons and others are preparing to sponsor study and advisory groups to cope with the problem of sex crimes. Of particular concern are the sex crimes against children and the control of the sex offenders. The solutions to the problems associated with this phase of community life are not easy to obtain. Nor are they confined to one group; they should be of interest to, among others, civic organizations, professional groups and law enforcement agencies. Well rounded programs will depend on cooperative study and planning. Members of the medical profession should be interested in community and even state or national efforts. Their participation will be important, and they can provide a real service to community life by assuming leadership when the latter is missing in areas in which sex crimes are the cause of much concern.

TRANSPORTATION OF NARCOTICS

Under the provisions of the Narcotic Drugs Import and Export Act, it is unlawful for a physician to carry narcotic drugs in his medical bag back and forth between the United States and Mexico and between the United States and Canada. Narcotic drugs found in the possession of a physician on returning to the United States are seized and forfeited. Because of lack of knowledge of the law, many physicians have been caused embarrassment and inconvenience when traveling between this country and Mexico or Canada. This information is published in order that physicians may be correctly informed with reference to this provision of the federal law.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

March 13, 1950.

Reforms May Result from Military Hospital Inquiry

Observers believe that significant changes, affecting civilian as well as military medicine, may result from the current congressional investigation precipitated by an order closing five Army and Navy hospitals and reducing 13 others in size. The investigating committee, headed by Chairman L. Mendel Rivers (Democrat, South Carolina), was scheduled to leave Washington March 13 on a 12 day inspection of the hospitals ordered deactivated by the Department of Defense. On the return of the House members, it will be decided whether public hearings will be continued on such questions as medical care of servicemen's dependents, relationship of military hospitals with medical schools, employment of civilian consultants, hospitalization of veterans in Army and Navy facilities and improved coordination of hospital construction planning.

The itinerary of the Rivers committee includes a one day visit to Percy Jones General Hospital at Battle Creek, Mich., followed by two days (March 15-16) in the San Francisco area, March 17-18 at Long Beach, Calif., March 19-20 at San Diego, March 22 at Corpus Christi, Texas, and March 23-24 at Augusta, Ga., with the party returning to Washington March 25. The tentative passenger list for the aerial tour included Representatives O. C. Fisher of Texas, Paul W. Shafer of Michigan, Clyde Doyle of California, Leroy Johnson of California and Chairman Rivers.

Medical Education and Science Foundation Legislation

Representative J. Percy Priest (Democrat, Tennessee), chairman of the House subcommittee on health legislation, has announced that his group has reached agreement on numerous changes in H. R. 5940, the bill on federal financial support of medical, dental and nursing schools and establishment of a scholarship system. He indicated that the measure would be submitted to the parent Committee on Interstate and Foreign Commerce during the week of March 13.

Conferences between House and Senate members to settle differences on National Science Foundation legislation were not expected to be scheduled before late March, because of the absence from Washington of Senator Elbert D. Thomas (Democrat, Utah), chairman of the Committee on Labor and Public Welfare.

Object to Social Security Law Changes

The Senate Finance Committee, conducting public hearings on proposed amendment of the social security laws, heard four medical witnesses on February 28 in opposition to compulsory contributory permanent and total disability insurance. They were Dr. James E. Paullin and Dr. R. L. Sensenich, past presidents of American Medical Association; Dr. Gunnar Gundersen, a member of the executive committee of AMA's board of trustees, and Dr. Bradford Murphey, representing the Colorado State Medical Society.

Dr. Dunham Heads AEC Medical Branch

The Atomic Energy Commission has announced appointment of Dr. Charles L. Dunham as chief of the medical branch, Division of Biology and Medicine, and establishment of the post of executive officer for the division. Named to that position is John A. Derry, who will assist the division director, Dr. Shields Warren, in matters relating to civilian defense, radiation instruments and general administration. Dr. Dunham, formerly assistant chief of the medical branch, succeeds Dr. John Z. Bowers, who has been made special assistant to Dr. Warren.

Medical Legislation

STATE LEGISLATION

Georgia

Bills Enacted.—H. 115 has become Governor's Act No. 691 of the Acts of 1950. It provides regulations for the organization and operation of **nonprofit medical service plan corporations.** H. 1056 has become Governor's Act No. 780 of the Acts of 1950. It amends the medical practice act relating to the **issuance of temporary licenses by** omitting the requirement of the existing law that the applicant must have been a practicing physician in a foreign state or country for at least twenty years.

Idaho

Bill Introduced.—H. 50-X proposes regulations for the **teaching of family relations** courses, including sex education and the essentials of good homemaking, in the public schools of the state.

Massachusetts

Bills Introduced.—H. 2054 proposes to authorize the department of correction to establish a clinic for the diagnosis and treatment of **alcoholics.** S. 533, to amend the law relating to nonprofit hospital service corporations, proposes to authorize **nonprofit hospital service corporations** to enter into reciprocal arrangements with other financially sound nonprofit hospital service corporations organized in other states to provide hospital service benefits for subscribers residing or employed in the commonwealth.

Mississippi

Bills Introduced.—H. 628 proposes an appropriation for the construction and equipping of **a four year medical school** to be operated as a part of the University of Mississippi. H. 630 proposes to authorize every inhabitant of the state of the age of 21 years or older to, by an instrument in writing executed as a deed and filed for record in the office of the county clerk, arrange for or prescribe for the **disposition to be made, after death,** of his body or any organ, member or part thereof, provided the disposition of the body or parts thereof is made for the purpose of advancement of medical science, or for the replacement of diseased or worn out parts of other humans or for the rehabilitation of human parts or other organs. H. 632 proposes to require all **drivers** of school buses to be examined by a competent physician and to present written certification that such person is **physically and mentally competent and fit to operate and drive a school bus,** the certificate to specifically include a statement that the vision and hearing of the operator is not so defective as to render him physically unfit to operate the bus. S. 463 provides, among other things, that whenever during the progress of any inquest it shall be deemed expedient by the coroner or justice of the peace that medical examination should be made, any competent doctor, surgeon or pathologist shall be summoned to make such **examination or autopsy and** for said services the doctor or pathologist shall be paid the sum of $50. If the doctor has to subsequently testify in any criminal proceeding his additional fee for so testifying as an expert shall be not more than one half of the above amount.

Bill Enacted.—H. C. Res. 45 was approved Feb. 22, 1950. It memorializes the representatives in the national Congress from the state of Mississippi to actively support the legislation providing for the setting up of a National Foundation for the study **of multiple sclerosis.**

New Jersey

Bills Introduced.—A. J. Res. 11 proposes the creation of a commission to study the problems and needs of **mentally deficient persons.** A. 318 proposes that a person duly authorized to practice medicine, surgery or dentistry, or a registered nurse, shall not be allowed or compelled to disclose in court or to any public officer any **confidential communication** or information which he acquired in attending a patient in a professional capacity and which was necessary to enable him to act in that capacity, unless the information so acquired indicates that the patient has been the victim or subject of a crime. A. 395 proposes to amend the medical practice act by permitting applicants to take the examination who show, in addition to other qualifications, that he was a **resident physician in** a county hospital in the state for twenty years. The provisions of this proposal would be in effect only until Jan. 1, 1952. A. 402 proposes that every physician shall report each case of cerebral palsy to the local board of health.

New York

Bills Introduced.—A. 2216 proposes the enactment of regulations providing a system of **prepaid medical and hospital care** and creating a health service fund in connection therewith. A. 2276 proposes the creation of a commission to investigate and analyze the nature and extent of **mental disorders and defects** and to study methods and procedures for the discovery, apprehension, custody, treatment, cure and rehabilitation of persons suffering from mental disorders and defects and of all other persons who are or may become a menace to society. A. 2342, to amend the education law, proposes to authorize the attorney-general to enforce **violations of the medical practice act** by the use of the injunctive process. A. 2409, to amend the insurance law in relation to **nonprofit medical and dental indemnity contract,** provides that the

medical expense indemnity shall consist of reimbursement for medical care provided through any duly licensed physician of the subscriber's choice, whether or not designated or approved by the corporation. A. 2679, to amend the penal code, proposes to make it unlawful for hospitals to refuse to admit and receive therein a person in need of **emergency care and treatment.** A. 2697, to amend the education law, proposes the creation of a state **board of examiners of psychologists** and defines a psychologist as one who renders to individuals or to the public any service involving the professional application of recognized principles, methods and procedures of the science and profession of psychology or who holds himself out as being able to or undertakes by whatever means to evaluate, appraise or classify mental abilities, personality characteristics, or personal or interpersonal maladjustments, or to perform psychologic reeducation, psychological readjustment, psychological guidance or counseling. A. 2708 proposes to make it **unlawful for any public or semipublic hospital,** supported wholly or partly by public funds, to refuse to permit any physician or surgeon duly licensed by the state to diagnose, treat or operate on any patient in any such hospital or to refuse admission to any such hospital of any patient who has been recommended to be sent to or who has been sent to any such hospital by any such physician or surgeon. A. 3047 proposes that no person, firm, association or corporation owning or operating a hospital, clinic, sanitarium or other similar institution shall permit the use or **operation of any ambulance for** the transportation to the institution of sick or wounded persons unless there is in attendance on such ambulance or vehicle at all times a duly qualified physician or intern who is a member of or connected with the staff of the institution. S. 1764 proposes the creation of a state **board of chiropractic examiners** and defines chiropractic as the science of locating and the removing of nerve interference in the human body, according to chiropractic principles where such interference is the result of or caused by misalignment or subluxations of the vertebral column. S. 1832 proposes the creation of a commission to make a study and survey of the prevalence and facilities for the treatment of all forms of **heart disease.** S. 1947, to amend the education law, proposes regulations relating to grievance committees and disciplinary actions against **physicians, osteopaths and physiotherapists.** S. 2191, to amend the public health law, proposes the enactment of a comprehensive statewide system of **health insurance.** S. 2223, to amend the administrative code, proposes to save harmless medical superintendents, deputy medical superintendents, lay superintendents and deputy lay superintendents of the department of hospitals from **liability** for their medical or administrative acts. S. 2229, to amend the education law, proposes that **a person practices medicine who** makes an examination, test or analysis of any fluid, excretion, secretion or tissue of the human body or of any organism contained therein where such examination, test or analysis is made for use or is used in connection with the diagnosis or treatment of any human disease, pain, injury, deformity or physical condition or for the confirmation of such diagnosis or treatment. S. 2238, to amend the education law, proposes to authorize the attorney general to make use of the injunctive process in enforcing the provisions of the **medical practice act.** S. 2244, to amend the penal law, proposes to authorize a surviving husband or wife or in the absence of such, an adult child, parent, a brother or sister or the relative or person undertaking the duty of burial or the decedent in writing during his lifetime to authorize an autopsy on his body after his death for the sole purpose of ascertaining **the cause of death.** S. 2246 proposes that plans for the setting up of health and medical centers shall include provisions for the establishment, maintenance and operation of a **school of medicine in the county of Bronx.** S. 2248, to amend the mental hygiene law, proposes regulations for the licensing of psychiatric clinics which is defined to mean and include mental hygiene clinic, child guidance clinic and other facility, by whatsoever name known, established or maintained by a public body, board, commission, official or by a membership corporation for the examination, diagnosis, care or treatment, on an out-patient basis, of persons suffering from **mental illness,** mental defect, epilepsy or behavior or emotional disorders. S. 2277, to amend the law providing for the creation of the office of county medical examiner in the county of Dutchess, proposes that if neither the medical examiner nor his assistant is a pathologist, then the board shall appoint an assistant county medical examiner whose only qualification for office and **duties shall be that of pathologist.**

Rhode Island

Bill Introduced.—H. 717 proposes to request the **Hospital Service Corporation of** Rhode Island (Blue Cross) to consider the feasibility of coverage for its subscribers when confined to private hospitals situated in and out of Rhode Island and broadening its benefits for such purpose.

South Carolina

Bills Introduced.—S. 45 proposes to require **applicants for a marriage license** to present a certificate signed by a duly licensed physician of his state certifying that the applicant is of sound mind and free from venereal disease in the contagious, infectious or communicable state.

Virginia

Bill Introduced.—S. J. Res. 21 proposes that the governing board of the Medical College of Virginia be requested to give consideration to permitting qualified Negro physicians to engage in their practice on their pay patients in St. Philip Hospital, one of the divisions of the Medical College of Virginia.

Bills Enacted.—H. 240 has become chapter 62 of the Laws of 1950. It provides for the creation of a Special Board of Examiners in Basic Science to examine chiropractors and naturopaths who now hold temporary licenses and sets up regulations how such chiropractors and naturopaths may obtain permanent licenses. H. 243 has become chapter 63 of the Laws of 1950. It permits the use of the injunctive process to prevent the unlawful practice of medicine, homeopathy, osteopathy, chiropractic, naturopathy or chiropody.

Coming Medical Meetings

Alabama, Medical Association of the State of, Birmingham, April 20-22. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Academy of Neurology, Cincinnati, Netherlands-Plaza Hotel, April 14-15. Dr. Joe R. Brown, Mayo Clinic, Rochester, Minn., Secretary.

American Association for Thoracic Surgery, Denver, Colo., April 15-19. Dr. Brian Blades, 901 Twenty-Third St. N.W., Washington, D. C., Secretary.

American Association of Anatomists, New Orleans, Louisiana State University, April 3-5. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

American Association of Industrial Physicians and Surgeons, Chicago, Hotel Sherman, April 24-28. Dr. Frederick W. Slobe, 28 E. Jackson Blvd., Chicago 4, Secretary.

American Association of Pathologists and Bacteriologists, Madison, Wis., April 14-15. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

American Association of Railway Surgeons, Chicago, Drake Hotel, April 4-6. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

American College of Physicians, Boston, April 17-21. Dr. George Morris Piersol, 4200 Pine St., Philadelphia, Secretary General.

American Gastro-Enterological Association, Atlantic City, April 28-29. Dr. Dwight L. Wilbur, 655 Sutter St., San Francisco, Secretary.

American Gynecological Society, White Sulphur Springs, W. Va., The Greenbrier, May 11-13. Dr. Norman F. Miller, 1313 E. Ann St., Ann Arbor, Mich., Secretary.

American Pediatric Society, French Lick, Ind., May 8-10. Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12, Secretary.

American Physiological Society, Atlantic City, April 17-21. Dr. Milton O. Lee, 2101 Constitution Ave., Washington 25, D. C., Executive Secretary.

American Psychiatric Association, Detroit, May 1-5. Dr. Leo H. Bartemeier, General Motors Bldg., Detroit 2, Secretary.

American Psychosomatic Society, Atlantic City, Chalfonte-Haddon Hall, April 29. Dr. Sydney G. Margolin, 714 Madison Ave., New York 21, Secretary.

American Society for Clinical Investigation, Atlantic City, May 1. Dr. Paul B. Beeson, Grady Hospital, Atlanta 3, Ga., Secretary.

American Society for Experimental Pathology, Atlantic City, April 11. Dr. Sidney C. Madden, Brookhaven National Laboratory, Upton, L. I., New York, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Atlantic City, April 17-21. Dr. Harvey B. Haag, Medical College of Virginia, Richmond 19, Secretary.

American Society of Biological Chemists, Atlantic City, April 9-14. Dr. R. W. Jackson, 825 N. University St., Peoria 5, Ill., Secretary.

American Surgical Association, Colorado Springs, Colo., April 19-23. Dr. Nathan Womack, University Hospitals, Iowa City, Iowa, Secretary.

American Therapeutic Society, Boston, April 13-16. Dr. Oscar B. Hunter, 915 Nineteenth St. N.W., Washington 6, D. C., Secretary.

Arizona State Medical Association, Phoenix, Hotel Westward Ho, April 30-May 1. Dr. Frank J. Milloy, 234 N. Central Ave., Phoenix, Secretary.

Arkansas Medical Society, Fort Smith, April 17-19. Dr. William R. Brooksher, 602 Garrison Ave., Fort Smith, Secretary.

Association of American Physicians, Atlantic City, May 2-3. Dr. Henry M. Thomas Jr., 1201 N. Calvert St., Baltimore 2, Secretary.

California Medical Association, San Diego, April 30-May 3. Dr. L. Henry Garland, 450 Sutter St., San Francisco, Secretary.

Connecticut State Medical Society, Waterbury, May 2-4. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Secretary.

Federation of American Societies for Experimental Biology, Atlantic City, April 17-21. Dr. Milton O. Lee, 2101 Constitution Ave., Washington 25, D. C., Secretary.

Florida Medical Association, Hollywood, April 23-26. Dr. Robert B. McIver, P. O. Box 1018, Jacksonville, Secretary.

Georgia, Medical Association of, Macon, Hotel Dempsey, April 18-21. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Hawaii Territorial Medical Association, Hilo, May 4-7. Dr. I. L. Tilden, Mabel Smyth Bldg., Honolulu 13, Secretary.

Iowa State Medical Society, Burlington, April 23-26. Dr. Allan B. Phillips, 406 Sixth Ave., Des Moines 9, Secretary.

Louisiana State Medical Society, Baton Rouge, April 24-26. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans 13, Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Baltimore, April 25-26. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

Mid-Atlantic Section, American Urological Association, Hot Springs, Va., The Homestead, March 23-25. Dr. H. N. Dorman, 1025 Connecticut Ave. N. W., Washington 6, D. C.

Mississippi State Medical Association, Jackson, May 9-11. Dr. T. M. Dye, Box 295, Clarksdale, Secretary.

Missouri State Medical Association, St. Louis, March 26-29. Dr. H. E. Petersen, 634 N. Grand Blvd., St. Louis 3, Secretary.

National Society for the Prevention of Blindness, Miami, Fla., Hotel Floridian, March 26-30. Dr. Franklin M. Foote, 1790 Broadway, New York 19, Executive Director.

National Tuberculosis Association, Washington, D. C., April 25-28. Dr. James E. Perkins, 1790 Broadway, New York 19, Managing Director.

Nebraska State Medical Association, Lincoln, Hotel Cornhusker, May 1-4. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln, Secretary.

New Mexico Medical Society, Las Cruces, May 4-7. Dr. H. L. January, 4852 Southern Ave., Albuquerque, Secretary.

New York, Medical Society of the State of, New York, May 8-12. Dr. Walter P. Anderton, 292 Madison Ave., New York 17, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, The Carolina, May 1-3. Dr. Millard D. Hill, 15 W. Hargett St., Raleigh, Secretary.

Northern Tri-State Medical Association, Grand Rapids, Mich., April 11. Dr. William H. Gordon, 1553 Woodward Ave., Detroit, Secretary.

Rhode Island Medical Society, Providence, R. I. Medical Library, May 10-11. Dr. Morgan Cutts, 106 E. Francis St., Providence 3, Secretary.

Tennessee State Medical Association, Memphis, April 10-12. Dr. W. M. Hardy, 706 Church St., Nashville 3, Secretary.

Texas, State Medical Association of, Fort Worth, May 2-5. Dr. Harold M. Williams, 700 Guadalupe St., Austin, Secretary.

GOVERNMENT SERVICES

ARMY

EMERGENCY MEDICAL PREPAREDNESS

To orient reserve officers on counter measures and treatments that would be entailed in atomic and bacteriologic attacks against this nation, and topics covering wide fields of emergency medical and health preparedness, a team of Army medical specialists will conduct contact camps in six large cities in the Second Army Area during March. Following is the itinerary of the 12 man team of specialists: Pittsburgh, March 8; Cleveland, March 11; Cincinnati, March 12; Baltimore, March 15; Philadelphia, March 16, and Richmond, Va., March 17. Medical reserve officers of the medical, dental, veterinary, medical service and Nurse and Women's Medical Service Corps are being invited to attend the seminars.

The Second Army is taking the seminar sessions to the field, so as not to infringe on the professional time of medical reserve officers by calling them to headquarters. A further convenience afforded by the seminar schedules is a 1:30 p. m. starting time.

SYMPOSIUM FOR RESERVISTS

The First Army is planning a three day Military Medical Symposium for members of the Organized Reserve Corps to be held at Governors Island, New York, April 26-28. Spaces have been reserved for 400 reservists, and invitations have been extended to the Navy and Air Force to send representatives. The program for the symposium will contain many distinguished military and professional leaders. Topics of major current interest and discussion panels on "Disaster Relief," "Current International Situation" and "ORC Affairs" are included in the program. Reservists desiring to attend the symposium may make application through their unit instructors.

Reserve officers from outside the metropolitan New York area under orders to attend will be paid for transportation, meals enroute ($1.25 per meal), meals while attending the symposium ($1 per meal) and quarters ($4 per day). Reservists living in the metropolitan area will be reimbursed only for meals. Retirement point credit will be given for attendance at the symposium.

AIR FORCE

ALASKAN MEDICAL ACTIVITIES

The Surgeon General, U. S. Air Force Medical Service, Major Gen. Harry G. Armstrong, and a group of 16 physicians and allied scientists recently visited medical installations in Alaska, conferred on medical problems and viewed medical and arctic survival equipment in actual use. Members of the group from the Office of the Surgeon General were: General Armstrong; Lieut. Col. Louis B. Arnoldi, chief, Career Control Branch; Lieut. Col. Walter J. Reuter, chief, Professional Branch, Air Force Dental Service; Major Frank G. Lord, Preventive Medicine Division; Major Robert R. Miller, Veterinary Division; Major John V. Painter, Medical Material Division, and First Lieut. Helen Ely, Air Force Nursing Service. From the Air Force Scientific Advisory Board were: Mr. Bernard J. Driscoll (Secretariat) and Dr. Edward J. Baldes. Members of the group from the Aero Medical Laboratory, Wright-Patterson Air Force Base, Ohio, were: Col. Walter A. Carlson, chief of the laboratory; Lieut. Col. A. P. Gagge, chief of operations, and Dr. John W. Heim, physiology branch. Brig. Gen. Earle Standlee, Army Medical Corps, represented the Office of Medical Services, Department of Defense. Lieut. Col. George M. Plagens represented the Military Air Transport Service, Andrews Air Force Base, Washington, D. C. Members from the USAF School of Aviation Medicine, Randolph Air Force Base, Texas, were: Lieut. Col. Ben Strickland, Department of Internal Medicine; Lieut. Col. Robert Lewis, Department of Pathology, and Dr. Albert Hetherington, Department of Physiology.

VACANCIES IN THE AIR FORCE

Public Law 216 extends the opportunity for transfer of officers between the Air Force Medical Service and the Army Medical Department until July 26, 1950. Vacancies in the Air Force Medical Service exist primarily in the Medical Corps and Nurse Corps. The Surgeons General of the Army and Air Force have in general been approving all requests for transfer of medical corps officers. Transfer of officers of other corps is limited to selected categories and are governed by requirements of the two services.

Officers assigned to medical installations where the Air Force and Army have joint staffing will normally complete their current tour of duty. Officers on duty at other type installations, however, will be transferred to the receiving department as soon as practicable. Reserve officers not on active duty are also eligible for transfer, subject only to the requirements of the departments. Applications should be initiated prior to June 1.

PUBLIC HEALTH SERVICE

THE NATIONAL HOSPITAL PROGRAM

More than a half billion dollars' worth of hospital and health center construction has been approved for government aid in the past twenty-five months, the Federal Security Administrator announced February 24. In addition to federal funds, this sum includes funds provided by the states, local communities and private organizations. Projects cleared by the Public Health Service over this period totaled 1,019 hospitals and health centers. They received a total of $210 million in federal funds. The first hospital approved for federal aid under the National Hospital Program was at Langdale, Ala., in November 1948; today 139 units are in operation, 523 under construction and 357 approved initially but still in the blueprint stage. Mississippi leads the nation with 83 projects, 9 of which are completed: Georgia lists 66, and Texas and South Carolina have 64 each. Projects in various stages are located in every state and territory. Completed hospitals are in operation in thirty-nine states. The National Hospital Program entails a survey of existing needs and the development of construction schedules on a priority of need. Federal aid up to $150 million annually is available on predetermined state allotments based on population and per capita wealth.

GRANTS FOR CANCER FACILITIES

Seven grants totaling $575,100 for the construction of cancer research facilities for universities, hospitals and other institutions have been announced by the Federal Security Administrator. The grants were approved by Surgeon General Leonard A. Scheele after recommendation by the National Advisory

Cancer Council. Five grants are for new projects and two are supplements to previous grants.

Following are grants for new projects:

North Carolina University, School of Medicine, Chapel Hill: Dr. W. R. Berryhill. $200,000 for cancer research facilities.

The Medical College of the State of South Carolina, Charleston: Dr. Kenneth M. Lynch. $100,000 to provide facilities for cancer research, including clinical investigation.

The Children's Medical Center, Boston: Dr. Sidney Farber. $100,000 to provide laboratory facilities for cancer research in the new building of the Children's Cancer Research Foundation.

Beth Israel Hospital, Boston: Dr. Charles F. Wilinsky. $50,000 to provide facilities for the care of laboratory animals required in cancer research.

State University of Iowa, College of Medicine, Radiation Research Laboratory, Iowa City: Dr. Titus C. Evans. $12,250 to provide improvements in laboratory facilities used for cancer research.

Grants to supplement previous grants were made to:

Wayne University, College of Medicine and Detroit Institute of Cancer Research, Detroit: Dr. G. H. Scott and Dr. William L. Simpson. $100,000 to supplement a previous National Cancer Institute grant of $150,000 for construction of cancer research facilities.

Boston University, School of Medicine, Boston: Dr. James M. Faulkner. $12,850 to supplement a previous National Cancer Institute grant of $49,900 for facilities for care of laboratory animals required in cancer research.

DENTAL DECAY—DEMONSTRATION TEAMS

Topical fluoride demonstration teams of personnel from the U. S. Public Health Service and supervised by the state departments of health are operating with the cooperation of dental societies and community organizations in thirty-eight states and territories including the District of Columbia. They demonstrate how a 2 per cent solution of sodium fluoride should be applied to the teeth of children to effect a reduction in new dental decay and show how locally sponsored communitywide fluoride programs might operate. Demonstrations have been conducted in schools in more than five hundred communities. At present, teams are operating in the following states and territories:

Alabama
Alaska
Arizona
Arkansas
Colorado
Connecticut
Delaware
District of Columbia
Florida
Hawaii
Illinois
Indiana
Kansas
Kentucky
Louisiana
Maine
Maryland
Massachusetts
Michigan
Missouri
Mississippi
Nevada
New Hampshire
New York
North Dakota
Oklahoma
Pennsylvania
Puerto Rico
Rhode Island
South Carolina
South Dakota
Tennessee
Vermont
Virginia
Virgin Islands
Washington
West Virginia
Wyoming

INFLUENZA STUDY PROGRAM

The list of Special Regional Laboratories for the World Health Organization influenza study program in the United States has been completed by the advisory committee comprising Dr. N. H. Topping (Public Health Service), Col. Don Longfellow (Army), Capt. R. W. Babione (Navy) and Major L. C. Kossuth (the Air Surgeon).

The Special Regional Laboratories are responsible for integrating the influenza study program for their respective areas. They enlist the assistance of other laboratories in the area, distribute specific influenza antigens and antiserums to their area collaborators and make final identification before influenza virus isolates are transmitted to the strain study Center at the Long Island College of Medicine, Brooklyn. The Collaborating Area Laboratories serve as look-out posts to report outbreaks of influenza; they perform red cell agglutination-inhibition tests with the serum of suspected cases, and in some cases they isolate virus from patients with influenza.

The physicians in charge of the program at each Special Regional Laboratory, the areas they serve and the Collaborating Area Laboratories in each region are as follows:

Boston City Hospital, Dr. Maxwell Finland	Region: New England
Collaborating Area Laboratories:	Yale University (Dr. E. C. Curnen) State Health Departments: Connecticut (Dr. F. E. Mickle) Massachusetts (Dr. R. F. Feemster)
New York State Health Department, Albany, Dr. Irving Gordon	Region: New York, New Jersey, Pennsylvania (Eastern), Delaware, Maryland, District of Columbia
Collaborating Area Laboratories:	Children's Hospital of Philadelphia (Dr. W. Henle and Dr. M. M. Sigel) Johns Hopkins University (Dr. T. G. Ward) Syracuse University (Dr. S. S. Kalter) New York City, P. H. Research Institute (Dr. G. K. Hirst) State and D. C. Health Departments: Dist. of Columbia (Dr. J. E. Noble) Maryland (Dr. C. A. Perry) New Jersey (Dr. J. H. Spooner)
University of Pittsburgh, Dr. Jonas Salk	Region: Pennsylvania (Western), Ohio, West Virginia
Collaborating Area Laboratories:	State Health Departments: Ohio (Dr. L. F. Ey) West Virginia (Dr. K. E. Cox)
University of Michigan, Ann Arbor, Dr. T. Francis	Region: Michigan, Indiana, Illinois, Wisconsin
Collaborating Area Laboratories:	University of Chicago (Dr. C. G. Loosli) Michael Reese Hospital, Chicago (Dr. A. Milzer) Navy Med. Research Unit No. 4, Great Lakes, Illinois State Health Departments: Illinois (Dr. H. J. Shaughnessy) Indiana (Dr. S. R. Damon) Wisconsin (Dr. W. D. Stovall)
State University of Iowa, Iowa City, Dr. A. P. McKee	Region: Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas, Wyoming, Colorado
Collaborating Area Laboratories:	St. Louis University (Dr. H. Pinkerton & Dr. G. O. Broun) State Health Departments: Minnesota (Dr. P. Kabler) Missouri (Dr. C. F. Adams) Nebraska (Dr. L. O. Vose) North Dakota (Dr. M. E. Koons) Wyoming (Dr. J. T. Ritter)
California State Dept. of Health, Berkeley, Dr. E. H. Lennette	Region: Montana, Idaho, Utah, Nevada, Arizona, Washington, Oregon, California
Collaborating Area Laboratories:	University of Oregon (Dr. A. W. Frisch) University of Washington (Dr. A. S. Lazarus) State and Territorial Health Departments: Territory of Alaska (Dr. E. P. Pauls) Territory of Hawaii (Dr. M. Levine) Los Angeles City (Dr. G. M. Uhl) Oregon (Dr. W. Levin)
U. S. Public Health Service Communicable Disease Center Virus Laboratory, Montgomery, Ala., Dr. M. Schaeffer	Region: Virginia, Kentucky, North Carolina, South Carolina, Tennessee, Georgia, Alabama, Mississippi, Florida, Louisiana, Arkansas, Oklahoma, Texas, New Mexico, and other state or local health departments which may wish to collaborate
Collaborating Area Laboratories:	Emory University (Dr. W. F. Friedewald) Louisiana State University (Dr. G. J. Buddingh) Southeastern Medical College (Dr. S. E. Sulkin) University of Tennessee (Dr. D. H. Sprunt) State Health Departments: Florida (Dr. A. V. Hardy) Louisiana (Dr. G. H. Hauser) North Carolina (Dr. J. H. Hamilton) Oklahoma (Dr. F. R. Hassler) South Carolina (Dr. H. F. Wilson) Texas (Dr. J. V. Irons) Virginia (Dr. A. Corpenning)
School of Tropical Medicine, San Juan, Puerto Rico, Dr. E. Perez	Region: West Indies
University of Toronto, Canada, Dr. C. E. van Rooyen	Region: Canada
Collaborating Area Laboratories:	Ontario Government Health Dept. (Dr. R. P. Hardman) Provincial Laboratories of Ontario (Dr. L. C. Barton)

FEDERAL AID TO MEDICAL EDUCATION

U. S. Public Health Service grants now aid cancer teaching programs in 76 of 79 medical schools in the United States and in 38 of the 41 dental schools. Grants totaling $522,181 for teaching cancer in 33 medical and dental schools in 20 states and the District of Columbia were recently announced. Cancer teaching grants awarded 20 medical schools in 15 states and the District of Columbia total $458,476. This includes one new grant of $25,000 to the Indiana University Medical Center, Indianapolis. The other 19 awards are renewals of previous similar grants. The grants were announced following approval by Surgeon General Scheele after they had been recommended by the National Advisory Cancer Council.

COURSES IN DIAGNOSIS OF TUBERCULOSIS

Three short courses in the laboratory diagnosis of tuberculosis will be given this year by the Laboratory Division of the Communicable Disease Center of the Public Health Service. The first, a one week course, will be held June 5-9. This will be followed by one of three weeks to be held August 21-September 8 and a two week course December 4-15.

Laboratory directors, senior staff members, physicians and employed laboratory personnel are eligible for the courses. Applicants from laboratories of state and local public health departments will be given first consideration, but applicants from hospitals and private laboratories will be eligible when vacancies occur.

There is no tuition charge or laboratory fee, but travel and living expenses must be paid by the individual or his employer. Applicants are requested to apply well in advance. Information may be obtained from the Chief, Laboratory Services, Communicable Disease Center, Public Health Service, Chamblee, Ga.

PERSONAL

Dr. Seward E. Miller has been appointed director of Public Health Service Region V with headquarters in Chicago. Dr. Miller has recently been chief of laboratory services in the Communicable Disease Center, Atlanta, Ga., and his successor in that position will be Dr. Ralph B. Hogan, who has been in charge of research for the public health service's Venereal Disease Division, Washington, D. C.

Dr. William H. Sebrell, director, Experimental Biology Medicine Institute, National Institutes of Health, was a member of the Joint Expert Committee on Nutrition of the Food and Agriculture Organization, which met recently in Geneva, Switzerland. During World War II Dr. Sebrell was co-director of the National Nutrition Program. He also helped draw up the first international standards of nutrition for the League of Nations.

Dr. T. Bruce H. Anderson, a medical officer of the Public Health Service for 35 years, retired March 1.

VETERANS ADMINISTRATION

ANNUAL NEUROPSYCHIATRIC MEETING

The third annual neuropsychiatric meeting at the Veterans Administration Hospital, Augusta, Ga., will be held March 31-April 1. Among others participating will be Drs. Foster Kennedy, New York; Robert S. Schwab, Lexington, Mass.; George H. Hyslop, New York; Eugene Davidoff, Schenectady, New York; Jacob L. Moreno, New York; John J. Blasko, Gulfport, Miss.; Edward J. Stieglitz, Washington, D. C., and Franz Kollman, New York. There will be no charge for registration, and all interested professional personnel are welcome. Information may be obtained from the Manager, Veterans Administration Hospital, Augusta, Ga.

HOSPITAL CONSTRUCTION PROJECTS

Twenty-six new Veterans Administration hospitals and six major additions to existing Veterans Administration hospitals are scheduled for completion during the calendar year 1950. These projects will contain about 11,710 new hospital beds and are under the supervision of the Veterans Administration Construction, Supply and Real Estate division and of the Corps of Engineers, Department of the Army. During the remainder of calendar year 1950, Veterans Administration plans to advertise 13 major hospital construction projects with a capacity of about 9,000 beds.

The Veterans Administration is accepting sealed bids for the construction of a 500 bed hospital in Cincinnati, which is to be built on a 19 acre site near the University of Cincinnati Medical School and near the Cincinnati General, Jewish and Children's hospitals. The construction project includes a main hospital building, nurses and staff apartment building, attendants' quarters, laundry building and boiler house. The buildings are to have concrete foundations, structural steel framing, brick-faced exterior walls with stone trim and backed with hollow tile, reinforced concrete floors and built-up roofs. Bids, prepared in triplicate on standard government forms of bid, must be received by the Director, Construction Service, Veterans Administration, Washington 25, D. C., by 1:30 p. m., March 28.

PERSONAL

Dr. Edgar C. Harper, tuberculosis control officer at Veterans Administration Hospital, Richmond, Va., has been transferred to the hospital at Mountain Home, Tenn., as chief of tuberculosis service and tuberculosis control officer. Dr. Harper, a veteran of World War I, at the Richmond Veterans Administration Hospital, developed the pilot program in which the Veterans Administration is attempting to set up methods of tuberculosis control within general hospitals. This is the first Veterans Administration assignment of a control officer in a hospital with a large domiciliary section.

Dr. Russell L. Hiatt has been appointed manager of the Veterans Administration hospital under construction at Fort Wayne, Ind. Dr. Hiatt will serve also as chief of professional services for the 200 bed hospital.

Dr. Glen W. Doolen, chief Tuberculosis Section of the Washington, D. C., Area Medical Office, has become manager of the Memphis, Tenn. (Lamar Avenue) hospital, succeeding Dr. Franklin C. Cassidy, who is being transferred to the Office of the Area Medical Director at San Francisco, Calif.

MISCELLANEOUS

NATIONAL AIR POLLUTION CONFERENCE

A national conference on air pollution—first government-sponsored conference of its kind—will be held in Washington, D. C., May 3-5, Secretary of the Interior Oscar L. Chapman announces. The conference, called at the suggestion of the President, will attempt to find solutions to the problems of atmospheric contamination. Secretary Chapman said that the conference is being sponsored by an interdepartmental government committee with various agencies participating in the conference. Dr. Louis C. McCabe, chief of Air and Stream Pollution, Bureau of Mines, chairman of the committee, is coordinating plans for the conference. Dr. J. G. Townsend, U. S. Public Health Service, and Dr. Robert A. Kehoe, Kettering Laboratories, Cincinnati, have been appointed chairman and co-chairman, respectively, of the panel on health.

In recent years, new industrial developments have created serious air pollution problems and federal agencies have been called on more and more to assist in finding a solution to these problems.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

COLORADO

State Health Council.—The Colorado Health Council, a nonprofit organization designed to obtain a complete health program in the state, was incorporated January 26 with 22 charter member organizations. The council will serve as a clearing house on health and medical care problems and programs, assist in the elimination of duplication and overlapping of effort in health and medical care programs and assist in the integration of such efforts, stimulate the formation of local and district health councils and bring together local and state wide organizations and agencies, governmental units and individuals to facilitate joint planning in the field of health. Members are voluntary and official agencies whose programs are state wide and are concerned entirely with health, county and district health councils and individuals interested in the purposes of the council. Mr. Mark Harrington, Denver attorney, was elected president and Dr. Monroe R. Tyler, Denver, of the state medical society, president-elect. Mr. J. P. Nordlund of the Colorado Medical Service is secretary. The council will secure an executive secretary in the near future.

DISTRICT OF COLUMBIA

New Hypertension Clinic.—The Georgetown new Hypertension Clinic opened February 17 at the Georgetown University Hospital, Washington, D. C. Dr. Edward D. Freis, Boston, has been named clinic chief. The clinic is open each Monday evening at 5:30 p. m. Those desiring to receive the benefit of its facilities will obtain a clinic pass from the Hospital Service Agency, 1823 L St., N. W., indicating eligibility and the amount the patient is to pay.

University Medical Society Award.—Dr. Daniel L. Borden, clinical professor of surgery at the George Washington University School of Medicine, Washington, received the University Medical Society's award of merit during the alumni reunion of the society February 25 at the Mayflower Hotel. Dr. Borden was presented a gold key and scroll "in recognition of his distinguished service and outstanding contributions to the field of medicine." As its recipient Dr. Borden became the university's medical alumnus of the year. His services include that of chairman of the Commission on Licensure of the District of Columbia, surgeon for the U. S. Employee's Compensation Commission, surgeon for the Police and Fire Clinic and chairman of the board since 1929, staff surgeon at Central Dispensary and Emergency Hospital and consultant at Children's Hospital, all in Washington. He serves the George Washington University also as director of health administration and university surgeon.

ILLINOIS

Mental Hygiene Meeting.—The annual meeting of the Illinois Society for Mental Hygiene will be held March 30 at the Standard Club in Chicago. Two section meetings will precede the luncheon, at which Dr. Daniel Blain, Washington, D. C., medical director of the American Psychiatric Association, will discuss: "Blueprinting Your Mental Health Program." Illinois Representative Bernice T. Vander Vries will lead the lay section, which will discuss what lay groups are doing in mental health. Dr. John P. Spiegel, chief of the psychiatric clinic, Michael Reese Hospital, Chicago, will preside over the professional panel of representatives in a discussion of the contributions professional groups are making to community psychiatry. The meeting is open to the public. Reservations may be made at the Illinois Society for Mental Hygiene, 123 West Madison Street, Chicago. The cost including luncheon is $2.75.

Chicago

Symposium on the Adrenal Gland.—The Chicago Urological Society will present a symposium on diseases of the adrenal gland March 23 at the Congress Hotel at 9 a. m. Drs. Rachmiel Levine and Ormand C. Julian will speak by invitation. A pyelogram clinic will be held from 11 to 12:30. An "Information Please" hour will follow the luncheon at 12:30. Visiting physicians will be Drs. James C. Sargent, Milwaukee; William N. Wishard Jr., Indianapolis, and John B. Wear, Madison, Wis. Papers will be presented at the evening meeting at 8 p. m., including one by Dr. George W. Wilson, who will speak on "Psychiatric Aspects of Genitourinary Symptoms."

Personals.—Dr. Loyal Davis, chairman, department of surgery, Northwestern University Medical School, has been appointed national chairman of a campaign to raise $500,000 for the Archibald Church Library at the medical school.——Dr. Archibald L. Hoyne has resigned as medical superintendent of the Chicago Municipal Contagious Disease Hospital; he was also medical superintendent of the Isolation (smallpox) Hospital and had held both positions for more than thirty years.

Alumni Lectures.—The alumni lecture series given by the Chicago Medical School in cooperation with Mount Sinai Hospital, will be continued through May 17. The series is open to all interested professional people and will be held on Wednesdays at 8 p. m. in the auditorium of the hospital. The remaining lectures are:

Israel Davidsohn, Clinical Application of the Rh Factor.
Archibald L. Hoyne, Practical Aspects of Contagious Diseases.
Peter Gaberman, The Lower Nephron Syndrome.
Milton Tinsley, Management of Head Injuries.
Harry J. Isaacs, Diagnosis and Management of the Pneumonias.
Albert Milzer, Present Status of the Virus Disease.
Aldo A. Luisada, Recent Advances in Cardiology—Part II.

A symposium on Newer Aspects of Thyroid Diseases will be presented May 17 by Drs. Piero P. Foa, Donald H. Atlas, Leo M. Zimmerman and David A. Willis.

MASSACHUSETTS

Cutter Lecture on Preventive Medicine.—The Harvard School of Public Health, Boston, announces that Douglas H. K. Lee, professor of physiologic climatology in the Isaiah Bowman School of Geography and lecturer in physiologic hygiene in the School of Public Health and Hygiene, both of Johns Hopkins University, Baltimore, will deliver the Cutter Lecture on Preventive Medicine on April 24 at 5 p. m. in Amphitheater D of the Harvard Medical School. His subject will be "Physiology as a Guide to Combating Tropical Stress." The medical profession, medical and public health students and others interested are invited.

Tufts Medical Alumni Meeting.—The Tufts Medical Alumni Association will hold its annual dinner meeting April 19 at the Somerset Hotel, Boston. The guest speaker is to be Chester I. Barnard, D.Sc., president of the Rockefeller Foundation and General Education Board, who will speak on "The Work of the Rockefeller Foundation." President Leonard Carmichael of Tufts College will speak on "Looking Toward the Future." Other talks will be given by Dean Dwight O'Hara and Dr. Harold G. Little, pathologist, Wheeling, W. Va. Dr. Frank R. Ober, Boston, will preside. The 25 year class will hold its reunion also on this date. Preceding the dinner there will be open house at the new Tufts College Medical School from 1 to 4 p. m.

MISSOURI

First Thompson Surgical Lecture.—The Thompson, Brumm and Knepper Medical and Surgical Clinic of St. Joseph, Mo., will inaugurate the F. G. Thompson Lectureship in Surgery on May 4 to honor 60 years of practice by Dr. Frederick G. Thompson, of St. Joseph. Dr. John M. Waugh, associate professor of surgery at the Mayo Clinic in Rochester, Minn., will speak on "Indications for Surgical Treatment of Peptic Ulcer."

Institute of Experimental Surgery.—The David P. Wohl Foundation of St. Louis recently granted $30,000 to the St. Louis University School of Medicine to establish the Wohl Memorial Institute of Experimental Surgery. The institute will also be utilized by various departments of the school of medicine and the staffs of Firmin, Desloge and St. Mary's hospitals; it will provide preoperative and postoperative wards, anesthetic, sterilizing and operating rooms and a diet kitchen.

NEW YORK

Teaching Day on Heart Disease.—The Rochester Academy of Medicine will present a postgraduate teaching day on heart disease for all physicians and medical students March 30 at the academy building. The program is as follows:

Harold M. Marvin, New Haven, Conn., Differentiation of Chest Pain.
Howard B. Sprague, Boston, Management of Cardiac Emergencies.
Edward F. Bland, Boston, Evaluation and Preparation of Poor Risk Cardiac Patients for Surgery.
George A. Perera, New York, Hypertension.

At 4 p. m. in a round table by previous speakers, questions submitted by the audience will be discussed. The program is being presented by the Heart and Rheumatic Fever Committee of the Health Association of Rochester and Monroe County, Inc., the local representative of the American Heart Association, in cooperation with Rochester Academy of Medicine and Medical Society of the County of Monroe.

New York City

Society Election.—At the annual meeting of the Brooklyn Urological Society the following were selected as officers for the year: Dr. Harold B. Hermann, president, and Dr. Andrew J. McGowan, Ozone Park, N. Y., secretary-treasurer.

Memorial Meeting.—A memorial meeting in honor of the late Dr. Robert T. Frank, consulting gynecologist to the Mount Sinai Hospital, will be held in Blumenthal Auditorium March 30 at 8:30 p. m. Dr. Morris A. Goldberger of the hospital, Dr. Edward A. Schumann, University of Pennsylvania, Philadelphia, and Dr. Emil Novak of the University of Maryland, Baltimore, will discuss Dr. Frank's contributions to gynecology and endocrinology. Dr. Frank died Oct. 15, 1949, aged 74.

Harvard Medical Alumni.—On April 13 the Harvard Medical Society of New York will hold its annual dinner meeting at the Harvard Club, 27 West 44th Street. President Conant and Dean George P. Berry, Boston, Mass., will be guests. The Harvard Medical Society is extending an invitation to Harvard Medical Alumni in New Jersey, Connecticut, Pennsylvania and New York State to attend this meeting. Dinner will follow a cocktail hour at 6:30. To nonmembers of the Harvard Medical Society of New York the price is $7.50.

Symposium on Congenital Cardiac Malformations.—A symposium on the diagnosis of congenital malformations of the heart will be presented at the New York Academy of Medicine Building April 5 at 8:15 p. m., sponsored by the New York Cardiological Society in conjunction with the Rudolf Virchow Medical Society in the City of New York and the New York University X-Ray Group. Participants will be Drs. Helen B. Taussig, Baltimore, and Arthur Grishman, Aaron Himmelstein and Charles E. Kossman. Members of the medical profession are invited.

OKLAHOMA

Course in Abdominal Surgery.—The department of surgery and the Division of Postgraduate Instruction of the University of Oklahoma School of Medicine, Oklahoma City, are holding their first postgraduate course in abdominal surgery. Dr. Champ Lyons, professor of surgery at the Medical College of Alabama, Birmingham, will be guest instructor. The course is primarily intended for Oklahoma physicians, and a registration fee of $15 for the three day course, April 6-8, is being charged.

PENNSYLVANIA

Tuberculosis Society Changes Name.—The Pennsylvania Tuberculosis and Health Society is the name adopted for the former Pennsylvania Tuberculosis Society. This is the second change in name since the society, reported to be the oldest citizen tuberculosis organization in the United States, was formed in 1892 as the Pennsylvania Society for the Prevention of Tuberculosis, which was changed in 1920 to the Pennsylvania Tuberculosis Society.

Prize for Paper on Thoracic Disease.—The Laennec Society of Philadelphia will give a prize of $200 for the best paper on thoracic disease submitted by an undergraduate medical student, intern or resident in Pennsylvania. The work should be original and not a review of literature or of previous contributions. The society does not reserve the right of publication but requests the prize-winning paper be presented at one of its regular scientific meetings. Manuscripts, double spaced with wide margins with bibliography and appropriate illustrations, should be in the hands of the secretary of the society, Dr. Katharine R. Boucot, 311 South Juniper Street, Philadelphia 7, Pa., by November 1.

Philadelphia

Personal.—Nearly 300 city officials, civic leaders, physicians and nurses honored Dr. Harriet L. Hartley, for 34 years chief of the division of child hygiene in the Philadelphia Bureau of Health, at a recent dinner on her retirement.

Medical Fraternity Lecture.—Dr. William Dameshek, professor of medicine at Tufts College Medical School, Boston, will deliver an address on "Hemolytic Anemia" at Klahr Auditorium of the Hahnemann Medical College, Philadelphia, March 30, at 8:30 p. m. This lecture is sponsored by the Phi Lambda Kappa fraternity at Hahnemann. All physicians and medical students are cordially invited.

Hospital Quarterly Journal.—The first issue of the *Journal of the Philadelphia General Hospital*, a quarterly published by the hospital, has appeared. It is edited by Dr. Pascal F. Lucchesi, superintendent and medical director, and a consulting board of editors including Drs. William P. Boger, Jefferson H. Clark, William E. Ehrich, Thomas M. McMillan, John F. Stouffer and Bernard P. Widmann. For information address Sholom O. Waife, M.D., associate editor.

Pittsburgh

Fracture Committee Meeting.—A meeting of the Regional Fracture Committee will be held in Pittsburgh at the Athletic Club April 13 at 2 p. m., with Dr. Wilton H. Robinson as chairman. Presentation of fracture problems by members or visitors by roentgenograms or cases will be held from 2 to 5:30 p. m. Following the dinner at 6 o'clock, Dr. Edward L. Compere, Chicago, will speak on "Segmental Fractures of Long Bones."

WISCONSIN

Industrial Health Clinics.—The State Medical Society of Wisconsin will conduct three industrial health clinics. The first, on April 13, will be held at the Kohler Manufacturing Company in Kohler. After a plant tour Dr. Ernest W. Miller, Milwaukee, will speak on "Treatment of Electric Burns"; Dr. William H. Frackelton, Milwaukee, "Treatment of Hand Injuries," and Dr. Clifford Kalb, Milwaukee, "Industrial Dermatosis." The dinner speaker will be Dr. Chester M. Kurtz, Madison, on "Managing the Cardiac in Industry." At the second clinic on April 30 at the Consolidated Water Power and Paper Company in Wisconsin Rapids, the same program will be presented. On May 3 the clinic will be held at the Globe Union Company in Milwaukee with the scientific program scheduled at the Plankinton Hotel. Dr. Elston L. Belknap, Milwaukee, will speak on "Toxic Solvents" and Dr. Harvey S. Allen, Chicago, on "Treatment of Hand Injuries." Dr. LeRoy H. Sloan, Chicago, as dinner speaker will discuss "Industrial Aspects of Heart Disease."

GENERAL

***Angiology*—A New Journal.**—The first number of *Angiology, The Journal of Vascular Diseases* appeared in February as a bi-monthly publication of the Angiology Research Foundation. The editor is Dr. Saul S. Samuels, New York, and the publishers are Williams and Wilkins Company, Baltimore. The first number includes eight scientific articles and an editorial. The Angiology Research Foundation is the recipient of any income derived from the new periodical together with that from other sources in the form of endowments. These funds will be used exclusively for the encouragement of research in problems related to vascular diseases. Subscription price is $8 per year, which should be sent to the publishers.

Southwest Allergy Forum.—This group will meet at the Hotel Peabody, Memphis, Tenn., April 2-4. Included in the program is a round table on "Antibiotic Therapy of Infectious Complications in Allergic States" with Dr. Loraine O. Dutton, El Paso, Texas, serving as moderator; another on "Nose and Throat Allergy" with Dr. Sam H. Sanders, Memphis, Tenn., as moderator; one on "Respiratory Allergy" with Dr. Jack Henry of Memphis as moderator, and on the final afternoon discussions on "Food Allergy" and "Antihistaminics" with Drs. Orval R. Withers, Kansas City, Mo., and Ethan A. Brown, Boston, the respective moderators. The registration fee is $10 for members and visitors with the exception of interns and exhibitors.

Industrial Health Conference in Chicago.—Teamwork in Industrial Health will be the theme of the annual meeting of the American Association of Industrial Physicians and Surgeons and four other industrial associations at the Sherman Hotel, Chicago, April 22-29. Registration is expected to exceed 2,000. The other groups are the American Industrial Hygiene Association, the American Conference of Governmental Industrial Hygienists, American Association of Industrial Nurses and the American Association of Industrial Dentists. More than 100 papers will be read. Section meetings will deal with general manufacturing, steel and heavy industry, petroleum, rubber and chemicals, hand and restorative surgery, workmen's compensation and insurance and the mining industry. On Monday afternoon and Tuesday morning there will be hospital clinics at St. Luke's and Cook County in Chicago. On Tuesday evening a symposium on alcoholism in industry will be presented. During the conference more than 20 large industrial plants in the Chicago area will have open house in their medical departments.

De Villiers Foundation Prize in Leukemia.—The Robert Roesler de Villiers Foundation, offers a prize of $500 for the paper which makes the most significant contribution to the knowledge of the nature, causes, origin, treatment or cure of acute leukemia and allied conditions. Should the paper be of outstanding importance, the prize may be increased to a maxi-

mum of $1,000. The prize-winning paper will be announced Oct. 20, 1951. Authors residing in countries outside the Western Hemisphere are requested to submit two copies of each paper to the Secretary-General, P. D. Sven Moeschlin, M.D., of the Societe Internationale Europaenne d'Hematologie, Kantonsspital, Zurich, Switzerland. Authors in countries of the Western Hemisphere are requested to submit their papers to the Secretary-General, Sol Haberman, Ph.D., of the International Society of Hematology, 3301 Junius Street, Dallas, Texas, U.S.A. Papers must arrive not later than April 30, 1951 in order to be eligible. The Robert Roesler de Villiers Foundation, Inc., is a membership corporation established under the laws of the State of New York exclusively for charitable, scientific, literary and educational purposes in memory of Robert Roesler de Villiers, who died of acute leukemia in 1944.

Annual Report of Committee on Growth.—The annual report of the National Research Council's Committee on Growth, covering the year ending June 30, 1949, reviews projects supported by $2,172,747 from funds contributed to the American Cancer Society by the public last year. The committee consists of 20 scientists who advise the society on allocating research funds for grants-in-aid and fellowships. The "Hormone Task Force" received $295,714, the largest portion of the society's project funds for 1949-1950. The committee termed the following developments "noteworthy research advances" in 1949: (1) new evidence relating to changes in blood serum of cancer patients; (2) evaluation of anti-folic acid compounds as a treatment of acute leukemia; (3) discovery of the potentialities of the hormones ACTH and cortisone and the preliminary testing of these drugs in cancer; (4) discovery of the new chemical compound guanazolo, and (5) further evidence that chemical agents which produce environmental cancer also cause changes in the hereditary pattern of the body's cells. In training are 54 American Cancer Society fellows. The committee recommended that the society approve appointment of 36 physicians as Damon Runyon Clinical Research fellows. The committee's report does not review the society's 1949 institutional research grants of $1,596,853, which brought the society's total allocations for cancer research to $3,769,600.

American College of Physicians.—The annual meeting of the American College of Physicians will be held in Boston April 17-21 under the presidency of Dr. Reginald Fitz, Boston, with headquarters at the Mechanics' Building. Physicians speaking by invitation include:

Karl F. Meyer, San Francisco, The James D. Bruce Memorial Lecture on Preventive Medicine: Global Strategy in Preventive Medicine.
Lord Moran, London, England, Wear and Tear.
Edward C. Kendall, Ph.D., Rochester, Minn., The John Phillips Memorial Lecture: Cortisone.
John P. Merrill, Boston, Role of the Artificial Kidney in Clinical Therapy.
Samuel Proger, Boston, Intractable Heart Failure.
Robert W. Wilkins, Boston, Effects of Various Physical Procedures on the Circulation in Human Limbs.
Lewis Dexter, Boston, Hypertension.
Kenneth A. Evelyn, Montreal, Canada, Long Term Study of the Natural History of Essential Hypertension.
John M. Weller, Boston, Clinical Problems of Potassium Metabolism.

Convocation will be held at 8:30 p. m. April 19 in the ballroom of the Hotel Statler. Ceremonies will include the president's address, "The Individuality of the American College of Physicians," and the Convocational Oration, "The Royal College of Physicians," by its president, Lord Moran. The annual banquet will be held on Thursday at 7 p. m.; James B. Conant, Ph.D., president of Harvard University, Boston, will be the dinner speaker. Morning lectures will be conducted on Wednesday and Friday and clinic sessions on Tuesday and Thursday from 9:15 to 11:30 a. m. Panel discussions are scheduled from Tuesday through Friday, 12 noon to 1:15 p. m. and will be held at Mechanics' Building and the Copley Plaza Hotel. A special feature will be a televised program from the Massachusetts General Hospital on Tuesday through Friday mornings.

Pharmacopeia Dedicates National Headquarters.—The dedication of the new headquarters of the Pharmacopeia of the United States at 46 Park Avenue, New York, will be April 12. The formal ceremony will be at 2:30 p. m. in the Hall of Morgan Memorial Library, just around the corner at 36th Street and Madison Avenue. The dedication program will consist of presentation of the building by the Board of Trustees to the officers of the U.S.P. Convention, represented by the President of the Pharmacopeia Convention, Dr. Cary Eggleston, New York. The five story building will provide permanent offices for the U.S.P. staff and appropriate space for the conferences which are now an integral part of the program of revising the pharmacopeia. Funds for purchase of the building were provided by individuals and organizations, whose business depends on the integrity of the Pharmacopeia standards. The United States Pharmacopeia was established in 1820. It is revised each five years by a national voluntary committee of medical and pharmaceutical experts and is accepted by Congress, under the Food, Drug and Cosmetic Act. Its standards are enforced by the Federal Food and Drug Administration and by many state and municipal health agencies. The dedicatory program includes addresses by Paul B. Dunbar, Ph.D., commissioner of food and drugs of Washington, D. C., and Dr. William G. Workman, director of the National Institutes of Health of Bethesda, Md.

International Congress on Obstetrics and Gynecology.—The International and Fourth American Congress on Obstetrics and Gynecology will meet at the Hotel Statler, New York, May 14-19. Speakers outside the United States who will present papers include:

Prof. Robert Courrier, College of France, Paris, Observations on the Physiology of Reproduction.
Prof. Carl Kaufmann, University of Marbury, Germany, Psychologic Factors Affecting Ovarian Function.
Prof. Hans Kottmeier, Radiumhemmet, Stockholm, Sweden, Therapy of Gynecologic Cancer.
Prof. Heinrich Martius, University-Frauenklinik, Gottingen, Germany, Treatment of Cancer of Cervix.
Prof. Leon Gerin-Lajoie, University of Montreal, Canada, Uterosalpingography in Differential Diagnosis of Uterine Bleeding.
Prof. Manuel Luis Perez, University of Buenos Aires, Argentina, Antibiotics in Obstetric Surgery.
Carlos D. Guerrero, Mexico, D. F., Conservative Management of Myoma Uteri.
Prof. Harold L. Sheehan, University of Liverpool, England, The Kidney in Abruptio Placentae.
Prof. Lakamanaswami Mudaliar, University of Madras, India, pathologic physiology of pregnancy.
Prof. Arnaldo de Moraes, University of Brazil, Rio de Janeiro, Total Hysterectomy in Non-malignant Conditions.
Toshio Hasegawa, University of Tokyo, Japan, Changing Incidence of Obstetric and Gynecologic Disorders During the War Years.
Prof. G. Dellepiane, University of Turin, Cytology of Malignant Cells.
Birger Lundquist, Stockholm, Sweden, Maternity Care in Sweden.
Marian Yang, Peking, China, Maternity Care in China.
Dorothy Taylor, British Ministry of Health, London, Evolution of the British Maternity Service.
Leonard Goodman, Maternity Hospital, Korle Bu. Accra, West Africa, Maternal Care in Africa.

Each paper is to be followed by a discussion. For registration and any other information address the chairman of the congress, Dr. Fred L. Adair, 24 West Ohio Street, Chicago 10. The General Program Committee chairman is Dr. Howard C. Taylor Jr., New York.

FOREIGN

Typhus in Japan.—According to telegraphic information received by the World Health Organization's Epidemiology Division at Geneva, a typhus epidemic is present in Japan and the country has been suffering from an outbreak of mild influenza. The situation, as reported, gives no cause for alarm. Tokio and Yokohama were the two places affected by the typhus epidemic. All passengers disembarking at Yokohama were required to present vaccination certificates. In Tokio about 150 confirmed or suspected cases were registered in the period January 15 to February 15 with a growing number of cases each week. Yokohama reported 26 suspected cases. Regarding the influenza situation, WHO reported, infection originating on Shikoku Island last December has spread throughout the country. The virus responsible was identified as B type.

CORRECTION

Lidocaine Hydrochloride.—In the monograph on lidocaine hydrochloride in THE JOURNAL, Feb. 4, 1950, page 341, the word "vasodepressor," in line 14 of Actions and Uses, should have been "vasopressor."

Marriages

PRESTON JOHNSON TAYLOR, Salt Lake City, to Miss Phyllis Wolcott Russell in New Haven, Conn., recently.

JAMES WILEY LYNN Jr., Belcher, La., to Miss Audrey Patrick Worthington of Grifton, N. C., December 28.

DENNIS P. MCCARTY, Delaplane, Va., to Miss Dorothy Mae Johnson in Washington, D. C., December 10.

CARLOS EUGENE RODRIGUEZ to Miss Virginia Marie Snow, both of Binghamton, N. Y., December 28.

ROBERT L. BUFFUM, Long Beach, Calif., to Miss Betty Frances Upham of Pacific Palisades, December 28.

JAMES TOLLIVER WORTHAM to Miss Jean Yvonne Biser, both of Durham, N. C., December 29.

CHARLES L. COLLINS to Dr. DELPHINE PALM, both of Vallejo, Calif., January 21.

Deaths

Otis Merriam Cope ✦ Gainesville, Fla.; born in Edmore, Mich., May 19, 1880; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; an affiliate Fellow of the American Medical Association; member of the American Physiological Society, New York Academy of Medicine, New York Academy of Sciences, American Association for the Advancement of Science, Harvey Society, Society for Experimental Biology and Medicine, New York Academy of Pathological Science and the American Heart Association; instructor in physiology at his alma mater from 1910 to 1918 and assistant professor from 1918 to 1924; associate professor of physiology and pharmacology at the University of Nebraska College of Medicine, Omaha, from 1924 to 1932; from 1932 to 1935 professor of physiology and physiologic chemistry and head of the department, New York Homeopathic Medical College and Flower Hospital and later, when it was known as the New York Medical College, Flower and Fifth Avenue Hospitals, served as professor of physiology and biochemistry; since 1948 acting professor of pharmacology and pharmacognosy, College of Pharmacy, University of Florida; died in Alachua Hospital January 28, aged 69, of cerebral hemorrhage.

Edmund Michael Van Buskirk ✦ Fort Wayne, Ind.; born in Monroeville, Ind., Feb. 11, 1875; Fort Wayne College of Medicine, 1902; past president and vice president of the Indiana State Medical Association; served as secretary, president and for many years councilor of the Twelfth District Medical Society; past president of the Fort Wayne Medical Society and the Indiana Roentgen Ray Society; from 1905 to 1922 county health officer; accepted a commission as captain in the medical corps of the U. S. Army during World War I; served as a member and president of the state board of health; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America and the American College of Radiology; affiliated with Lutheran Hospital and Methodist Hospital, where he died January 18, aged 74, of aplastic anemia.

James Rae Arneill ✦ Denver; born in De Pere, Wis., in 1869; University of Michigan Medical School, Ann Arbor, 1894; professor emeritus of medicine at the University of Colorado School of Medicine; formerly on the faculty of his alma mater; fellow of the International College of Surgeons and the American College of Physicians, of which he had been a member of the board of regents; specialist certified by the American Board of Internal Medicine; served during World War I; affiliated with Swedish National Sanatorium, Englewood, Mercy, St. Anthony, St. Joseph's, Beth Israel, Children's and St. Luke's hospitals; author of "Clinical Diagnosis and Urinalysis"; contributor to "Reference Handbook of the Medical Sciences"; died in Orlando, Fla., January 27, aged 80, of intestinal obstruction.

Charles Frederick Adams ✦ Jefferson City, Mo.; born in Atherton, Mo., April 4, 1877; Kansas City Medical College, 1902; acting director, Division of Health of Missouri; formerly director of the division of laboratories of the state board of health, a position he held for many years; at one time director of the state laboratories of the Indiana State Board of Health; specialist certified by the American Board of Pathology; member of the American Society of Clinical Pathologists and the American Public Health Association; fellow of the Conference of State and Provincial Public Health Laboratory Directors; formerly taught at the universities of Arkansas, Kansas and Chicago; at one time pathologist at St. Mary's Hospital; died January 21, aged 72, of intracranial hemorrhage and carcinoma of the prostate.

Samuel Dinwiddie Weaver ✦ Dallas, Texas; born in Pontotoc, Miss., Nov. 1, 1887; Tulane University of Louisiana School of Medicine, New Orleans, 1916; clinical professor of surgery at Southwestern Medical College; formerly on the faculty of Baylor University College of Medicine; past president of the Texas Surgical Society; fellow of the International College of Surgeons and the American College of Surgeons; member of the National Gastroenterological Association; served in France during World War I; affiliated with Baylor Hospital, Methodist Hospital, Medical Arts Hospital and the Parkland Hospital, where he died January 20, aged 62, of carcinoma.

Edward Lyman Cornell ✦ Chicago; Rush Medical College, Chicago, 1910; served as assistant professor of obstetrics at Northwestern University Medical School; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons and the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; past president of the Chicago Gynecological Society; past secretary of the Maternal Welfare Committee of Cook County, which he helped found; formerly on the staffs of the Chicago Lying-In Hospital and Passavant Memorial Hospital; since 1934 head of the department of obstetrics at Henrotin Hospital, where he died January 31, aged 66, of coronary occlusion.

Charles Chauncey Winsor Judd ✦ Baltimore; born in Bound Brooke, N. J., in 1883; Johns Hopkins University School of Medicine, Baltimore, 1911; formerly on the faculty of the University of Maryland School of Medicine; past president of the Baltimore City Hospital; at various times served on the staffs of Mercy, St. Joseph's and the South Baltimore General hospitals, all in Baltimore, Peninsula Hospital in Salisbury, Md., and the Emergency Hospital in Easton; member of an advisory board during World War I; died in the Union Memorial Hospital January 19, aged 66, of myocardial infarction.

Charles Leslie Aker, Greencastle, Ind.; Indiana University School of Medicine, Indianapolis, 1923; member of the American Medical Association; died December 2, aged 56.

Levi Franklin Anderson, Buffalo; University of Buffalo School of Medicine, 1907; member of the American Medical Association; died recently, aged 67, of acute dilatation of the heart.

James Smith Bates ✦ Lake Preston, S. D.; Louisville (Ky.) Medical College, 1901; died February 2, aged 74, of coronary thrombosis.

Walter A. Bell, Vanleer, Tenn.; University of Nashville (Tenn.) Medical Department, 1911; member of the American Medical Association; died January 13, aged 62, of coronary thrombosis.

Roscoe Paramore Blood, Hebron, Ind.; Northwestern University Medical School, Chicago, 1906; died in Porter Memorial Hospital, Valparaiso, December 2, aged 69, of carcinoma of the liver.

John Hiram Bowen, Cobbtown, Ga.; University of Georgia Medical Department, Augusta, 1894; member of the American Medical Association; died December 4, aged 83, of bronchopneumonia.

Elwyn Temple Butterfield, Las Vegas, N. M.; State University of Iowa College of Medicine, Iowa City, 1937; member of the American Medical Association; served during World War II; specialist certified by the American Board of Ophthalmology; affiliated with St. Anthony's Hospital and Las Vegas Hospital; died January 22, aged 40, of pulmonary embolus.

Julius Cantala ✦ New York; Universidad Literaria de Valladolid Facultad de Medicina, Spain, 1911; Long Island College Hospital, Brooklyn, 1927; died in Madrid, Spain, January 30, aged 60, when the automobile in which he was riding collided with a bus.

David E. Cantrell, Healdton, Okla. (licensed in Oklahoma under the Act of 1908); member of the American Medical Association; affiliated with Hardy Sanitarium, Ardmore; died recently, aged 73, of cerebral hemorrhage.

James Jefferson Carter, Columbus, Ohio; Meharry Medical College, Nashville, Tenn., 1921; member of the American Medical Association; died in Grant Hospital January 3, aged 51, of injuries received when struck by an automobile.

Robert Wanee Chambers ✦ Beckley, W. Va.; Jefferson Medical College of Philadelphia, 1925; certified by the National Board of Medical Examiners; served as a member and president of the county board of education; died February 9, aged 53, of brain tumor.

George Lincoln Chapman, Santa Ana, Calif.; Rush Medical College, Chicago, 1894; died January 21, aged 80, of cerebral hemorrhage.

Amable Albert Comeaux, Abbeville, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1913; served during World War I; affiliated with Abbeville Clinic Hospital; died January 17, aged 63, of coronary thrombosis.

Francis Wayland Davis, Cincinnati; Miami Medical College, Cincinnati, 1891; died January 28, aged 81, of chronic myocarditis.

Lee Roy Doolin, Gallatin, Mo.; Barnes Medical College, St. Louis, 1898; died January 11, aged 83, of chronic nephritis.

Edward Deal Finch ✦ Howell, Mich.; University of Michigan Medical School, Ann Arbor, 1936; member of the American Trudeau Society; director of the out-patient department of the Michigan State Sanatorium; died January 31, aged 42, of myocardial infarction.

✦ Indicates Fellow of the American Medical Association.

Edward Otto Foss, Muskegon, Mich.; Hahnemann Medical College and Hospital, Chicago, 1906; past president of the Muskegon County Medical Society; member of the American Medical Association; for many years on the staff of Mercy Hospital, where he died January 8, aged 68.

Dennis Luther Fox, Randleman, N. C.; Vanderbilt University School of Medicine, Nashville, Tenn., 1894; company surgeon, Southern Railway; died in the Yadkin Hospital, Albemarle, January 16, aged 81, of obstruction of the bile ducts, probably due to metastatic melanoma.

Nathan Edward Friedman, Cleveland; University of Wooster Medical Department, Cleveland, 1900; served on the staff of St. Alexis Hospital; died January 22, aged 72, of cardiac hypertension.

James Thomas Frizzell, Clinton, Okla.; Kansas City (Mo.) Medical College, 1900; member of the American Medical Association; for many years city and county health officer; affiliated with Western Oklahoma State Hospital, where he died December 5, aged 79, of coronary sclerosis.

Ernest Almore Gauvain ✦ Glen Cove, N. Y.; Long Island College Hospital, Brooklyn, 1918; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; formerly on the faculty of his alma mater; served on the staffs Swedish, Lutheran, Kings County and Caledonian hospitals, all in Brooklyn; on the staff of North Country Community Hospital, where he died January 18, aged 56.

Ezra Edward Geisel, Tucson, Ariz.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; died January 23, aged 71, of hypostatic pneumonia.

Janet B. Clarke Gibson, Longmont, Colo.; Denver Homeopathic College, 1900; member of the American Medical Association; affiliated with the Longmont Hospital and Clinic; died January 7, aged 72, of carcinoma.

Victor Lee Gilmore, Los Angeles; Medical Department of Tulane University of Louisiana, New Orleans, 1889; died January 23, aged 87.

Edward M. Glaser ✦ Brookville, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; for many years president of the Franklin County Tuberculosis Association; past president of the Fayette Franklin Counties Medical Society; county health officer; president of the People's Bank; died January 18, aged 67, of coronary heart disease and hypertension.

Roy Mark Greenthal ✦ Milwaukee; University of Michigan Medical School, Ann Arbor, 1918; formerly on the faculty of his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; affiliated with Milwaukee Children's Hospital and Columbia Hospital, where he died January 27, aged 54, of cerebral hemorrhage and hypertension.

Frank John Hager, Denmark, Wis.; Milwaukee Medical College, 1911; member of the American Medical Association; served during World War I; for many years health officer; died in Green Bay January 5, aged 67, of cerebral hemorrhage.

Sherwin Livingston Haseltine, Griggstown, N. J.; Kansas City (Mo.) Hahnemann Medical College, 1914; served during World War I; formerly practiced in Elizabeth, where he was on the staffs of the Elizabeth General, Alexian Brothers and St. Elizabeth's hospitals; died January 28, aged 64, of uremia.

Harry Hausman ✦ Daytona Beach, Fla.; University and Bellevue Hospital Medical College, New York, 1908; died January 8, aged 64, of rheumatic heart disease.

Nathaniel A. Herring, Niles, Mich.; Bennett Medical College, Chicago, 1880; member of the American Medical Association; past president of the Berrien County Medical Society; died January 28, aged 93, of senility.

Lorin L. Hewitt, Dayton, Ore.; Willamette University Medical Department, Salem, 1907; died January 18, aged 80, of coronary occlusion.

Wright Platt Hewitt ✦ Cambridge, Mass.; Harvard Medical School, Boston, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the New England Oto-Laryngological Society; affiliated with Cambridge City and Mount Auburn hospitals; died February 2, aged 43, of rheumatic heart disease.

Robert Asa Hills ✦ Russell, Iowa; College of Physicians and Surgeons, School of Medicine of the University of Illinois, 1907; past president of the Lucas County Medical Society; died in Des Moines January 4, aged 67, of paralysis agitans.

Albert Sidney Johnston, Springfield, Mo.; American Medical College, St. Louis, 1897; member of the American Medical Association; while practicing in Wheatland was a charter member and the first president of the Dallas-Hickory-Polk Counties Medical Society; died in St. John's Hospital January 14, aged 77, of arteriosclerotic heart disease.

John Joseph Kelly, Marlboro, Mass.; Tufts College Medical School, Boston, 1904; member of the American Medical Association; retired school physician; affiliated with Marlboro Hospital, where he died December 20, aged 71, of coronary occlusion.

Charles V. Kraft, New Orleans; Kentucky School of Medicine, Louisville, 1897; died November 14, aged 78, of cerebral hemorrhage and arteriosclerosis.

William Franklin Lehr, Arlington, Ohio; Eclectic Medical Institute, Cincinnati, 1899; served as member and president of the school board; affiliated with the Findley (Ohio) Hospital; director of the Farmers and Merchants Bank; died January 13, aged 79, of cerebral hemorrhage.

James Parker MacDowell, Dundee, N. Y.; University of Vermont College of Medicine, Burlington, 1904; member of the American Medical Association; school physician; for many years coroner and health officer; past president of the Yates County Medical Society; member of the staff of the Soldiers and Sailors Memorial Hospital at Penn Yan; died January 25, aged 70, of sarcoma of the abdominal wall.

Haden Edwards McKay, Humble, Texas; Louisville (Ky.) Medical College, 1894; member of the American Medical Association; served as health officer; died December 1, aged 79, of coronary occlusion.

George Benjamin Norberg ✦ Kansas City, Mo.; University Medical College of Kansas City, 1897; served on the faculty of his alma mater; an Associate Fellow of the American Medical Association; affiliated with St. Mary's Hospital and Trinity Lutheran Hospital, where he died January 23, aged 77, of acute coronary thrombosis and carcinoma of the tongue.

John Bernard O'Connor, Oelwein, Iowa; State University of Iowa College of Medicine, Iowa City, 1896; died in Mercy Hospital, January 20, aged 75, of cardiac arteriosclerosis.

Leon Hardy O'Quinn, Hialeah, Fla.; Emory University School of Medicine, Atlanta, 1923; member of the American Medical Association; in 1935 mayor of Hialeah; city physician; affiliated with Jackson Memorial Hospital and Victoria Hospital in Miami; formerly surgeon for the Florida East Coast Railway; died December 12, aged 51.

Lena Rosamond Holmes Waite, Perrysburg, N. Y.; University of Buffalo School of Medicine, 1923; resident physician at the J. N. Adam Memorial Hospital; died in General Hospital, Buffalo, January 15, aged 62.

Samuel C. Webster, Chester, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1890; also a graduate in pharmacy; formerly practiced in Westerly, R. I., where he was township health officer for many years and was affiliated with Westerly Hospital; died January 6, aged 87, of arteriosclerosis.

Oscar G. Wernicke, Chicago; Rush Medical College, Chicago, 1889; member of the American Medical Association; died in Wesley Memorial Hospital February 23, aged 87, of pulmonary emphysema.

Joseph Gilbert Whitacre ✦ Lodi, Ohio; Ohio State University College of Homeopathic Medicine, Columbus, 1917; served during World War I; on the staff of Lodi Hospital; died January 7, aged 62, of carcinoma of the pancreas.

Daniel H. Wiesner, Mamaroneck, N. Y.; University of the City of New York Medical Department, New York, 1880; member of the American Medical Association; served on the staff of the Manhattan Eye and Ear Hospital in New York; died January 26, aged 90.

William Bronnie Wild ✦ Pasadena, Texas; University of Oklahoma School of Medicine, 1925; died December 20, aged 51.

Samuel Smart Williams, Angola, La.; Memphis (Tenn.) Hospital Medical College, 1911; served during World War I; affiliated with the medical department of the Louisiana State Penitentiary; died January 16, aged 66, of pulmonary hemorrhage and shock as the result of an automobile accident.

James M. Willis ✦ McCook, Neb.; Central Medical College of St. Joseph, Mo., 1903; fellow of the American College of Surgeons; served as city health officer; affiliated with St. Catherine of Sienna Hospital; died January 8, aged 68, of coronary occlusion, hypertension and polycystic kidneys.

Barnett Edgar Winters, Columbus, Ohio; Starling Medical College, Columbus, 1896; member of the American Medical Association; affiliated with White Cross Hospital; died January 6, aged 82, of arteriosclerotic heart disease.

Foreign Letters

LONDON

(From a Regular Correspondent)

Jan. 24, 1950.

The Amending Act

The National Health Service Act became law Nov. 6, 1946. However, the "appointed day" for those parts of the Act which most closely concern the medical profession was deferred until July 5, 1948.

On Dec. 16, 1949 the National Health Service (Amendment) Act became law. The first part of this Act clarifies the position of medical partnerships and removes some ambiguities and obscurities in the original Act to which attention was drawn by the profession's representatives sitting as the old Negotiating Committee as long ago as December 1947.

The main provisions of the 1949 Act may be summarized as follows:

1. Effect is given to the recommendations of the Legal Committee on Partnerships.

2. A full time salaried family physician service is prohibited (with an exception for special circumstances).

3. A full time salaried dental service except in health centers is prohibited.

4. The act prohibits the imposition by regulation of any universal whole time specialist service.

5. It provides for the arbitration of disputes on the remuneration or conditions of service of those engaged in the health service.

6. The Minister of Health is required to make regulations providing for the removal from executive council lists of medical and dental practitioners, chemists and opticians who have never provided or have ceased to provide services for a particular executive council area.

7. It authorizes the Minister to make regulations: (*a*) extending the functions of the Medical Practices Committee; (*b*) requiring patients receiving general medical or dental services to pay part of the cost of drugs and appliances prescribed (with the power to exempt certain classes); (*c*) providing for charges to be made for the use of the service by specified classes of persons not ordinarily resident in Great Britain, and (*d*) limiting the certificates which a doctor may be required to issue free of charge to his National Health Service patients.

8. It empowers the Minister to authorize the provision of medical services privately at health centers, subject to conditions which he will determine.

9. Executive councils are now given the right to select their own chairman.

10. It empowers executive councils on the request of the local professional committee to make statutory deductions from the remuneration of doctors, dentists, chemists or opticians to defray the administrative expenses of those local professional committees.

11. It makes provision for the professional member of the tribunal under Section 42 of the Act to be selected from a panel of available members.

12. It defines a new "appointed day" for members of a partnership who have not joined the health service to do so and receive compensation.

Amending Regulations

A number of equally important alterations are embodied in the National Health Service (General Medical and Pharmaceutical) Service Amendment (no. 2) Regulations, 1949.

FREE CERTIFICATES

These regulations include a provisional list of certificates which a doctor is now required to issue free of charge to his National Health Service patients. This list has been agreed on by the General Medical Services Committee. Further amending regulations are necessary before the present list can be extended. It is made clear in the regulations that a doctor is not required to issue certificates to his patients who are receiving treatment from unqualified persons. The accompanying tabulation is a list of these free certificates.

FILLING VACANCIES

Perhaps the most significant change effected by the new regulations (reports the Secretary of the British Medical Association in the Supplement to the *British Medical Journal* of January 14) is that relating to the filling of vacancies arising from the death, retirement or removal of a general practitioner on the list. A distinction is now made between an application for inclusion in the medical list and an application to fill a "practice declared vacant." In neither the original Act nor the regulations was any distinction drawn between the function of the Medical Practices Committee in selecting a candidate for a particular vacancy and those in admitting to the list a practitioner for the purpose of starting a practice in the area.

The transfer of patients of an outgoing practitioner to another practitioner on the list has hitherto been effected by the executive council without the permission of the Medical Practices Committee. The effect of the new regulation is to give the Medical Practices Committee the last word in determining whether or not a vacancy should be filled and by whom it should be filled. Previously the committee could declare an area "closed," but this operated only to prohibit additions to the medical list. In future it will be for the Medical Practices Committee (or, on appeal, the Minister) to select the doctor to fill a declared vacancy, even if the applicant is already on the executive council's medical list. It follows that all doctors whose applications are refused, including unsuccessful applicants who are already on the list, will be entitled to appeal.

Free Certificates

Medical Certificate	Short Title of Enactment Under or For the Purpose of Which Certificate Required
To support a claim or obtain a payment either personally or by proxy under the enactments specified	Family Allowance Act, 1945 (8 & 9 Geo. 6 c. 41); National Insurance (Industrial Injuries) Act 1946 (9 & 10 Geo. 6 c. 62); National Insurance Act 1946 (9 & 10 Geo. 6 c. 67)
To prove inability to work or incapacity for self support for the purposes of an award by the Ministry of Pensions. To enable proxy to draw pensions	Pensions (Navy, Army, Air Force and Mercantile Marine) Act, 1939 (2 & 3 Geo. 6 c. 83) Pensions (Mercantile Marine) Act 1942 (5 & 6 Geo. 6 c. 26); Naval and Marine Pay and Pensions Act, 1865 (28 & 29 Vict. c. 73); Air Force (Constitution) Act 1917 (7 & 8 Geo. 5 c. 51); Personal Injuries (Emergency Provisions) Act 1939 (2 & 3 Geo. 6 c. 82); Polish Resettlement Act 1947 (10 & 11 Geo. 6 c. 19).
To procure: (*a*) extra coal in cases of illness; (*b*) extra milk; (*c*) extra petrol, and (*d*) extra rations	Emergency Powers (Defence) Acts 1939-1945, as having effect by virtue of the Supplies and Services (Transitional Powers) Act, 1945 (9 & 10 Geo. 6 c. 10) and Supplies and Services (Extended Purposes) Act 1947 (10 & 11 Geo. 6 c. 55)
To obtain permission to import foreign drugs and appliances; to obtain permission to export special foods with sick traveler or with infant 2 years of age or under	Import, Export & Customs Powers (Defence) Act, 1939 (2 & 3 Geo. 6 c. 69)
To enable patient to have his sight tested under the Supplementary Ophthalmic Services	National Health Service Act 1946 (9 & 10 Geo. 6 c. 81)
To establish fitness to receive nitrous oxide and air analgesia in childbirth	Midwives Act 1902 (2 Edw. 7 c. 17)
To secure registration of stillbirth	Births and Deaths Registration Act 1926 (16 & 17 Geo. 5 c. 48)
To enable payment to be made to another person in case of mental disability of person entitled to payment from public funds; to justify release of patient from detention after absence on trial	Lunacy Act, 1890 (53 & 54 Vict. 3.5)
To establish unfitness for jury service	Juries Act 1922 (12 & 13 Geo. 5 c. 11)
To establish unfitness to attend for medical examination	National Services Act 1948 (11 & 12 Geo. 6 c. 64)
To support late application for reinstatement in civil employment where application delayed by sickness	Reinstatement in Civil Employment Act, 1944 (7 & 8 Geo. 6 c. 15)
To enable a disabled person to be registered as an absent voter	Representation of the People Act 1949 (12 & 13 Geo. 6 c. 68)

Moreover, the new regulations embody the understanding that, when a selection has been made by the Medical Practices Committee (or, on appeal, by the Minister) to fill a death or retirement vacancy, the patients of the outgoing doctor shall be transferred to the doctor selected unless the committee (or the Minister) decides otherwise. The patient's right to change to another doctor is, of course, retained.

The duty of reporting to the Medical Practices Committee on the necessity to fill vacancies remains with the executive council and the local medical committee, but when exceptionally the Medical Practices Committee disagrees with the local point of view the Minister has asked executive councils to defer to the view of the Medical Practices Committee, since that body is charged with the task of controlling distribution.

NEW OPPORTUNITY TO ENTER SERVICE

Under the 1946 Act each family physician who wished to join the Service had to enroll before July 5, 1948 and could claim compensation for the loss of the saleable "goodwill' of his practice. Anyone joining after that date could not claim such compensation. The Amending Act gives members of a partnership in existence on July 5, 1948 who have not joined the Service the opportunity of entering the Service with the same compensation rights as applied to those who entered on the originally appointed day, by applying to the appropriate executive council within two months of the passing of the Amending Act, i.e., before Feb. 16, 1950. Partners in this position will be entitled automatically to be included on the medical list by sending Form E. C. 16 to the executive council. The application need not be considered by the Medical Practices Committee.

EMPLOYMENT OF ASSISTANTS

Under the new regulations a doctor who has been refused the consent of the executive council to employ an assistant may appeal to the Medical Practices Committee. A principal who employs an assistant is given the right to have his list increased by another 2,400 patients, (to a maximum of 6,400 patients), if the Minister so decides. (This prevents an executive council from prohibiting a doctor's doing this, as has happened on one occasion.)

Assistants may no longer have their names on the medical list. Exceptions to this are: (*a*) part time assistants who are also practicing separately as principals on their own account, and who in the latter capacity can build up lists of their own; and (*b*) assistants whose names are included in the medical list of an area before February 1.

BULK PRESCRIBING FOR SCHOOLS AND INSTITUTIONS

A medical practitioner responsible for the treatment of not less than 10 persons in a school or institution in which at least 20 persons are normally resident may now issue a bulk prescription for drugs but not for appliances for 2 or more of those residents for whom he is not receiving a dispensing capitation fee. The prescription may contain only those drugs which are included in the National Formulary, other than those to which the Dangerous Drugs Acts apply and those which are or contain Fourth Schedule poisons.

FEES FOR PUBLIC HEALTH MEDICAL OFFICERS

For considerably more than a year the British Medical Association has been pressing for the opening of negotiations with the government (through what is called the "Whitley machinery") for new scales of public health doctors' remuneration. At long last it is possible to announce that the first meeting of the Medical Functional Council of the National Health Service Whitley machinery will take place on January 26. Among the steps which will be taken at that meeting will be the establishment of Committee C, the Public Health Committee, which will begin discussions on new scales of remuneration for the public health officers. Within the ambit of the committee will fall not only medical officers of local health authorities but medical officers of local authorities which are not local health authorities.

As regards the present remuneration of Medical Officers of Health, a correspondent to the *British Medical Journal* of January 14 quotes the following advertisements:

> Wanted—A County Sanitary Inspector. Salary $2,240 per annum.
>
> Wanted—Assistant Anaesthetist } Both consultant status, and salary
> Wanted—Assistant Radiologist } $4,760 to $7,700 per annum.
>
> Wanted—Clerk of the . . . . shire Executive Council. $2,842 to $3,430 per annum salary in accordance with the scale approved by the Minister of Health.
>
> Wanted—Assistant County Medical Officer (preferably with a higher postgraduate qualification or degree or a Diploma in Public Health). Salary $2,058 per annum.

These serve to stress the present anomalous position, and it is hoped that some agreement will soon be reached.

Mr. Ewing's Recent Visit

A British weekly periodical comments on Mr. Ewing's recent visit from America. It states that Americans are surprised to find that so many of those British doctors who opposed the introduction of the National Health Service are actually in the Service and apparently trying to make it work successfully. It is hinted that in doing so they are trying to make the best of both worlds. The *British Medical Journal* points out that "the real explanation is nothing so sinister. It is rooted in the contrariness, the illogicality, the what-you-will of the British temperament, and the ineradicable capacity to make the best of things. It is a case of not merely bowing to the inevitable but of shaking the inevitable by the hand and working with the inevitable in the hope of eventually, if not exactly transforming the inevitable, at least of bringing about a mutual accommodation and a working arrangement satisfactory to both sides."

It does not point out that the vast majority were forced into the Service by means of economic pressure (a polite word for "blackmail"); that many are in the Service with a great sense of grievance and frustration; that the spirit of ill will which exists between a large proportion of the profession and their governmental masters could have been avoided; that had they failed to join practically all consultants and specialists would have been robbed of all or almost all their public ward and private beds. It fails to distinguish between the doctors' good will towards their patients and the "apparently" trying to make the Service work successfully and does not mention the "spanners in the works." Nor does it give expression to the faith in each man's heart that change and decay will have their natural effects and that the age long spirit of the freedom of medical practice will eventually triumph over bureaucracy.

BRAZIL

(From a Regular Correspondent)

RIO DE JANEIRO, Jan. 25, 1950.

Progress Against Malaria

Great progress has been registered in Brazil in the fight against malaria during the last two years. The results of the survey carried out by the Malaria Division of the National Department of Health, during 1947 and the beginning of 1948, showed that of the 1,780 counties of Brazil malaria was present in 1,196 (67.2 per cent), in the large majority of them endemically, with moderate or slight gravity, and in the rest in the form of periodic epidemics of variable extent and severity, which in some instances developed also in the endemic areas. The endemic and epidemic manifestations of the disease spread over almost all the Atlantic seaboard (about 3,800 miles) and the valleys of the great and small rivers. Free from malaria are

only the littoral of Rio Grande do Sul—the southernmost state with the coolest climate, where the disease is a problem in only two Atlantic counties, the semiarid inland districts of the bulge states (Ceará, Rio Grande do Norte, Pernambuco and northern Bahia), the southern and southeastern sections of Minas Gerais, most of the Paraíba river valley in the state of Rio de Janeiro and some small isolated areas in several parts of the country. According to conservative reasonable estimates, a minimum of 6,000,000 persons are affected by malaria every year (12,867 per hundred thousand population), with about 65,000 deaths directly attributed to the disease (13.8 per hundred thousand). Until 1938 the antimalarial activities of the federal government were practically limited to cooperation with state authorities in stamping out the most important outbreaks of the disease. Since 1938 the federal government has assumed a much greater part in the antimalarial work, which was confined to the areas around the large cities. The only really important achievements of the 1938 to 1940 period were the complete eradication of the African mosquito vector Anopheles gambiae, which was imported from the African region of Dakar by way of the rapid means of communication developed through the South Atlantic, and the great work of dredging rivers and digging ditches in the Baixada Fluminense (more than 3,000 square miles of lowlands to the north and east of the Federal District). The eradication of the Anopheles gambiae from the states of Rio Grande Norte and Ceará, where it had been left to take root and spread for several years, was a great medical feat carried out by a joint American-Brazilian antimalaria special service, described in 1943 by Drs. Fred L. Soper and D. Bruce Wilson of the Rockefeller Foundation ("Anopheles Gambiae in Brazil—1930 to 1940"), who singled out the great work performed by Dr. M. J. Ferreira, a distinguished Brazilian malariologist and administrator.

In 1941 a specialized service was created in the National Department of Health—the Division of Malaria—with a large autonomy, to combat the disease in all Brazil except in the Amazon basin and in part of the Rio Doce valley. These regions constituted the particular field of the SESP (Special Service of Public Health—a third of the expenditures of which are covered by American money from the Institute of Inter-American Affairs), and in the state of São Paulo, where the work was under the jurisdiction of the state department of health. The Malaria Division progressively increased the work against the mosquitoes of the subgenus Nyssorhynchus, using the classical methods of antilarval measures, through hydraulic sanitation work, and the application of paris green and petroleum, aiming at the destruction of the breeding places of anophelines. The Malaria Division has completed several large projects, mainly directed to the protection of the malarial areas around the large cities and the localities where the Brazilian (and during the war also the American) armed forces were stationed. The antimalarial protection of the great Brazilian-American air bases at Natal, Recife and Salvador, state of Bahia, are notable examples of this kind of work, continued afterward around the military bases located near São Luis, state of Maranhão, Aracajú, state of Sergipe, and Santos, state of São Paulo. Up to 1947 the Malaria Division built more than 450 miles of ditches and more than 35 miles of deep drains and surfaced with concrete more than 350 miles of ditches. During the period 1941 to 1947 more than 100 million cubic feet of earth were moved to fill low places, pits and swamps. However, the results of this great work were not always sufficiently rewarding.

This situation was greatly changed when effective measures against adult mosquitoes were possible by the advent of chemicals of residual toxic effect. Since 1942 spraying walls and ceilings of houses with DDT has revolutionized the malaria control work. In 1946 the Malaria Division obtained enough DDT to try the new method on an experimental scale, spraying 6,419 houses. The real work with DDT began in 1947, when two great projects were started: the house spraying of the São Francisco river valley (states of Bahia, Sergipe and Alagoas), and that of the rural areas of the entire state of Rio de Janeiro, which surrounds the Federal District. At the close of the year 186,189 houses had been sprayed with DDT, 130,419 of which were in the state of Rio de Janeiro. Much was still to be done, as the number of houses in the malarial areas of the country were estimated at about 3 million, which would take more than ten years to be sprayed at the pace then prevailing. Tons of DDT were bought, thousands of sprayers and hundreds of vehicles of every type (trucks, jeeps, launches and small airplanes) were spread over different parts of the country, accompanied by numerous personnel of every type, including about eighty physicians. At the end of 1948 the number of houses protected reached 968,611, a part of this total having received, during the year, the second or third spraying. While new cycles of spraying were continued in the valleys of the São Francisco and Tocantins rivers and in the state of Rio de Janeiro, new projects were started including the Federal District and all the states with the exception of Amazonas, Pará and Ceará. During the year 1949 the work continued in the same seventeen states and the Federal District, and a new project was begun in Ceará. In the whole of this area about 2.4 million houses were sprayed one, two and three times, requiring more than 2,000 tons of DDT, about 1.3 million gallons of solvents and emulsifiers, 501 jeeps and trucks, 10 launches and 21 airplanes. Since Jan. 1, 1950 the antimalarial work in the Amazon valley, which was performed by the special Service of Public Health, and that in the state of São Paulo, administered by the State Department of Health, have passed under the jurisdiction of the Malaria Division, which has now the full responsibility of protecting about 3.5 million houses with some 20 million people in rural areas throughout Brazil. This is a population equivalent to that of Argentina or to that of Bolivia, Ecuador, Paraguay, Uruguay and Venezuela combined. This impressive program of spraying so many houses with DDT puts Brazil in the leadership of all the world nations in malarial control. The steady growth of this particular work is well revealed by the progressive increase of the appropriations voted to cover its cost in the last five years: 1945, U. S. $2,562,600 (0.60 per cent of the federal budgeted expenditures); 1946, $4,515,200 (0.91 per cent); 1947, $5,832,300 (0.92 per cent); 1948, $7,118,100 (0.93 per cent), and 1949, $11,029,900 (1.07 per cent).

Another phase of the antimalarial work done on a large scale by the Malaria Division is the treatment of patients with chloroquine, which is not intended as a prophylactic treatment but rather as a measure of social welfare, by the immediate stopping of the clinical manifestations of the disease, thus avoiding the interruption of the persons' activity. This objective is attained by the administration of one dose of 1 Gm. of the drug for adults and a proportionally reduced dose for children. The drug is distributed without charge to the patients by more than 16,000 stations installed in schools, farms, town halls, churches, post-offices and railroad stations, in order that any person may obtain the drug at the maximum distance of 4 miles from his residence. During 1949 more than a million people were treated with chloroquine furnished free by the large network of distributing stations.

Otorhinolaryngology and Bronchoesophagology

Dr. Julio C. Barani, of Montevideo, Uruguay, stayed a few days at Rio de Janeiro and São Paulo, as the executive secretary of the second Pan-American Congress of Otorhinolaryngology and Broncho-Esophagology, to be held at Montevideo January 8-15. Dr. Barani is visiting all the American nations, to invite representatives to one of the most important meetings of that specialty. During the week of the congress a few short

courses on subjects related to otorhinolaryngology and bronchoesophagology will be given by prominent specialists. Among these courses there will be one on otosclerosis, by Drs. George E. Shambaugh, John Londsay and H. Kobrak, of Chicago; one on plastic surgery, by Dr. John M. Converse, of New York City; one on the pathology of the sinuses of the face, by Drs. Romeu Luongo of Philadelphia and Ermiro Lima of Rio de Janeiro, and one on endoscopy, by Drs. Chevalier Jackson of Philadelphia, Paul H. Holinger of Chicago and P. M. Barretto of São Paulo.

Control of American Trypanosomiasis

A division of Rural Endemic Diseases will be created at the National Health Department within the next few months to cooperate with the local organizations in the control of hookworm disease, intestinal schistosomiasis, American trypanosomiasis, frambesia and other tropical diseases. While waiting for the organization of the new division, the Malaria Division of the National Health Department, which is doing antimosquito work in large areas where American trypanosomiasis is endemic, has been directed to intensify the campaign against the insects with dichlorodiphenyltrichloroethane (DDT), which is approximately as effective against the Reduviidae as against mosquitoes. The Minister of Health recommended that, with the cooperation of the Oswaldo Cruz Institute, a more complete plan be prepared to begin a campaign against the vectors of trypanosomiasis (Chagas' disease).

Brief Items

As directed by a recent law passed by the Brazilian Congress, the federal government granted to the Escola Paulista de Medicina, a private medical school of the city of São Paulo, a subsidy of 28,000,000 cruzeiros ($1,400,000) to cover the expenses of completing its general hospital and laboratories. The Escola Paulista de Medicina, founded 15 years ago, is the second institution of the kind at the city of São Paulo. The older medical school is one of the units of the University of São Paulo.

Dr. Narno Dorbecker, head, department of radiology of the Institute of Cardiology, Mexico City, spent a few days in São Paulo as a guest of the university of that city. Among other activities, Dr. Dorbecker delivered a lecture on the radiologic and angiocardiographic aspects of the persistence of the arterial canal, the coarctation of the aorta and the interauricular communication. For several years Dr. Dorbecker, who is a pioneer in angiocardiography, has been studying the dynamic radiology of the heart. He recently read to the third Inter-American Congress of Cardiology held at Santiago, Chile, a paper on his studies on that subject.

Dr. Oswald S. Lowsley, director of the department of urology (Brady Foundation) of the New York Hospital, arrived at Rio de Janeiro as a guest of the Hospital of Public Servants. Dr. Lowsley lectured at the hospital on modern problems of urologic surgery.

The annual meeting of the Brazilian Radiological Association was held recently in Salvador, state of Bahia, with a large attendance of Brazilian specialists and several radiologists from Europe and other South American countries. Among the guests were Drs. Manuel Malenchini, Alfredo Givré, Roberto Alvarez, Lidio Mosca and Sabino Di Rienzo, all of Argentina; Dr. Quirino Quodas, Paraguay; Dr. Rudolf Pape, Australia; Dr. Raymond Laterjet, France, and Dr. Juan J. Scandroglio, Uruguay.

Dr. Gregorio Bermann, professor of psychiatry at the University of Cordoba, Argentina, spent a few days at Rio de Janeiro, as a guest of the Institute of Psychiatry of the University of Rio. He delivered two lectures on "Contemporaneous Antagonism Between Mental Diseases and Other Diseases."

COLOMBIA

(From a Regular Correspondent)

Jan. 20, 1950.

Rural Public Health

Law 03842 of the government of Colombia requires all medical students who obtain an M.D. degree to work for one year on rural public health in different territories of Colombia. In fulfilment of this law the physicians who graduated last year will carry on work on rural sanitation. The total number of graduate physicians in Colombia is 3,327. The number of patients for every physician will exceed 3,000. About 2,065 physicians practice in capital cities, whereas people in rural territories lack a sufficient number of physicians. Of the total number of persons who die in Colombia in a year, 88,000 persons die without having had medical care. There are physicians in only 370 of the 815 municipalities of Colombia, and there have never been physicians in the other 445 municipalities. Data obtained from the Ministry of Public Hygiene disclose that 65 per cent of the total population of the country receives medical care and the remaining 35 per cent does not.

Dr. Jorge E. Cavelier, secretary of public hygiene, sponsored law 03842, which establishes one year of obligatory service on rural sanitation for all pregraduate physicians from this year on. This period of service is equivalent to the year of medical practice which is included in the course of studies at the state medical schools. The schools in which the physicians finished their medical studies will give them their M.D. degree as soon as they finish a year of rural service according to the law. The municipalities will pay honorariums to the physicians, which will vary between 400 and 800 Colombian pesos. The amount is designated in accordance with climate and cost of living in the given municipalities. The same law is in force for pregraduate dentists. The first group of 300 physicians who will give rural service now are taking a special course on hygiene and will begin their duties March 1, 1950.

Foreign physicians and dentists who are graduated from universities in countries not having international agreements with Colombia for recognition of their diplomas are allowed to practice medicine and dentistry, respectively, provided they apply to the Ministry of Hygiene for an appointment for rural service for three years.

Brucellosis

Drs. Luis Patiño Camargo, Andrés Soriano Lleras and Rafael Colmenares recently reported before the National Academy of Medicine on their studies on brucellosis in Colombia. Infectious abortion of cattle was officially reported in the Department of Bogotá, in 1927. The epizootic has been reported at the present time in one hundred and fifty-two municipalities of eleven Departments of Colombia. By means of vaccination and other preventive measures brucellosis has decreased in some of the previously infected territories, whereas it had completely disappeared in others. The incidence in human beings is alarming.

The authors performed seroagglutination tests on samples of blood from 1,743 persons living in rural areas, especially those who were in contact with cattle and animal products. The group of persons from rural zones of twelve Departments of Colombia included adults and children between the ages of 7 and 80 years. Positive results were obtained in 4.6 cases per hundred. There were 59 positive reactions in the group of 1,206 men and boys and 22 cases in the group of 537 women and girls. The percentage of positive results was higher in slaughterhouse workers, butchers and milkers. The highest index of infection was obtained in persons between the ages of 31 and 40 years. The highest degree of positivity was obtained in persons living in the Departments of el Valle, Cundinamarca and Caldas with rates of 16.5, 10.8 and 10.5 cases per hundred, respectively.

The clinical diagnosis of brucellosis is more frequent now than formerly, and the results of the biologic tests are confirmatory of the clinical diagnosis. During the courses on tropical medicine which were given in Bogotá the patients were observed by the students.

Correspondence

TESTS FOR OCCULT BLOOD IN FECES

To the Editor:—Reference is made to the article, "Clinical Evaluation of Various Tests for Occult Blood in Feces," by Stanley O. Hoerr and associates in THE JOURNAL, Dec. 24, 1949, page 1213. This paper recommends the use of the guaiac test for routine office practice. Few clinical pathologists will share this opinion.

Many occult blood-producing diseases, among them gastric carcinoma, are often the silent types and only the finding of certain blood elements in the stool will arouse a suspicion of malignancy.

The authors recommend the old Weber test for blood, yet the guaiac test as routine test or screening test was abandoned more than twenty-five years ago. Many modifications followed: the guaiac was replaced by aminopyrine, Meyer's reagent, orthotoluidine and benzidine. Each of these had a common fault; lack of specificity and either too much or too little sensitivity.

In cases in which clinical evidence of gastrointestinal ulceration is present the occult blood test gives 20 per cent negative results; this is due to the fact that the peroxydase was destroyed by the presence of pus, putrefaction or other causes and there is no trigger left to release the reaction. No one should undertake examination for occult blood without first examining microscopically the feces for meat fibers, potato starch and green vegetable rests.

In the decomposition of blood through intestinal passage the hematin is not necessarily the most important factor. There is porphyrin also. This porphyrin is not reacting to guaiac or other color-producing reagents, yet it is present in 100 per cent of gastric ulcerative malignancies. To detect hematin, porphyrin, chlorophyll and other pigments there is only one specific and sensitive method, and that is the spectroscopic examination, in which all the proper absorption bands are specific and easily read.

There is no reliable substitute for this spectroscopic test in occult blood examination, and it should be used more extensively in hospital laboratories, where at the present it is a sort of stepchild.

C. M. MEZEY, M.D., Station B, Gulfport, Miss.

To the Editor:—Dr. Mezey's criticism of the flaws in the guaiac test, from the standpoint of a perfect means for detecting blood in the feces, are well taken. It seems to me, however, that he has missed the chief point of the paper, namely, the development of a test which is reasonably accurate and yet so simple that the busy practitioner can still perform it in his office. The test for occult blood has many clinical uncertainties connected with it. As Dr. Mezey points out, the very lesions that one would hope to detect by such a means not infrequently fail to bleed enough to produce a positive reaction to a test. We had hoped to make clear in our paper that a negative test for occult blood in the stool should never be taken as sound evidence against a gastrointestinal lesion when there was other good reason to suspect its presence. It was our thought that by placing one additional diagnostic aid in the hands of the family physician an occasional case of otherwise unsuspected gastrointestinal disease would be detected. We believe that the test offers such a possibility, and beyond that our claims for it are modest.

STANLEY O. HOERR, M.D., Columbus, Ohio.

CAUTION IN USING DESOXYCORTICOSTERONE

To the Editor:—Since the advent of cortisone and pituitary adrenal corticotropic hormone (ACTH) for some of the arthritides, some physicians have been eager to use preparations of the adrenal cortex in treatment of this disease. Some of us recently have been subjected to pressure from medical detail men to use adrenal cortical extracts and desoxycorticosterone acetate. These men sometimes have less scientific knowledge than ability to sell. We, as physicians, have to be extremely careful during a new trend of therapy, that we do not succumb to excessive enthusiasm.

One piece of medical advertising that has come to my attention constitutes the poorest form of medical journalism I have yet seen. Apparently a few articles in medical literature in which desoxycorticosterone acetate was used for rheumatoid arthritis with claims of relief are the basis of the article. The writer evinces enthusiasm in the article in an attempt to sell the product, but he also carefully leaves himself some loopholes for retraction. We of the medical profession should follow not medical trends but specific scientific work that has been established. Desoxycorticosterone acetate is not a substitute for cortisone or pituitary adrenal corticotropic hormone.

Desoxycorticosterone acetate has been used in treatment of Addison's disease. It has a powerful sodium-retaining reaction and can cause sodium retention and water retention to the point of edema, hydremia and death. There have been reports that the use of desoxycorticosterone acetate has caused subacute arthritis with fever and increased sedimentation rates. This has definitely supported the experimental work of Selye, who produced arthritis in animals by administering desoxycorticosterone acetate.

I believe that pharmaceutical companies should watch their salesmen and themselves in their sales methods of exploitation of medical practitioners and the public, particularly when arthritis is the disease to be treated. Physicians must not forget what happened in the overenthusiastic use of massive doses of vitamin D.

DAVID S. RAUSTEN, M.D., Lincoln 6, Neb.

TRANSFUSION WITH POSITIVE PRESSURE

To the Editor:—It has come to my attention that a commercial firm manufacturing and distributing transfusion apparatus sells with the apparatus a bulb and attachment in order to create a positive pressure in the bottle for the purpose of increasing the speed of the transfusion. This practice must be strongly condemned because in the past it has caused death from air embolism.

Since transfusions are prescribed today almost as freely as saline solution, the blood transfusion practice should be as foolproof as possible. Transfusing blood with the aid of air under pressure is certainly not foolproof (Wiener, A. S.: "Foolproof" Blood-Transfusions, *Lancet* 1: 1073 [June 18] 1949). The manufacture and sale of transfusion apparatus such as the one described, which constitutes an unnecessary hazard to the life of the patient, should be discouraged. In cases in which blood must be transfused rapidly, this can be accomplished safely by inserting a three way valve between the cannula and the intravenous tubing and pumping the blood in at the desired speed by syringe.

A. S. WIENER, M.D.,
New York.

Medical Motion Pictures

FILM REVIEWS

Rickettsiae. Laboratory Procedure for Their Isolation and Identification (PMF 5114). 16 mm., color, sound, showing time forty-seven minutes. Produced in 1949 by the United States Army. Procurable on loan from the Army Surgeon of the Army area in which the request originates.

This motion picture was designed for students taking a basic science course. It is a photographic record of a laboratory procedure. The film is long and detailed and gives the slow, step by step demonstration of the technic of laboratory diagnosis of rickettsial disease. Gross pathology is well demonstrated and compared with the normal. The rickettsiae are well shown. The following fundamentals are emphasized: sterile technic; handling infected laboratory animals; drawing blood from the heart of a guinea pig; details in performing postmortem examination of a guinea pig; cleansing hands with alcohol; protecting abrasions on the skin; freezing of tissue and blood, and packing of blood samples for transportation. The demonstration is plain, logical and complete. There is some repetition, especially in performing necropsies on normal and infected guinea pigs. In the comparison of pathologic tissue with normal tissue, the normal is on the left under Rocky Mountain spotted fever and on the right under murine typhus.

This film would serve as a good review for students in basic science, bacteriology and in the second year of medical school. At the beginning of the film a chart is photographed. Apparently this material was originally prepared for an exhibit, and it did not reproduce well on 16 mm. film. This material should have been redone, perhaps in color, especially for use in this film. In general the photography is good.

Time Out: Occupational Therapy in Tuberculosis. (PMF 5116A). 16 mm., black and white, sound, showing time twenty-seven minutes. Produced in 1949 by the United States Army. Procurable on loan from the Army Surgeon of the Army area in which the request originates.

This motion picture, designed primarily to show how effective occupational therapy can be, portrays the experiences of a young man who finds himself obliged to enter a hospital for the treatment of pulmonary tuberculosis. Many general aspects of his hospital life are shown, but the emphasis is on the usefulness of properly planned occupational therapy in keeping the patient cheerful and in preparing him for the return to normal life. The dialogue is pointed and witty, and the cast is well selected.

This film should be of primary interest to hospital personnel. It may also be shown to the patient who is being oriented in a hospital for tuberculosis or to the type of patient who becomes restive during a long period of hospitalization and needs to be convinced of the need for patience. Group showings of this film might greatly aid the efforts of hospital authorities to get their patients oriented and to win their cooperation. It should also have great value to audiences of many nonprofessional adult groups.

Script writing and direction of this motion picture are excellent, as are the photography and narration. There is human interest and cleverness in the way the film is put together.

Breast Cancer: The Problem of Early Diagnosis. 16 mm., color, sound, showing time thirty-five minutes. Scientific supervision and sponsorship jointly by National Cancer Institute and American Cancer Society. Produced in 1949 by Audio Productions, Inc., New York. Procurable on purchase from the American Cancer Society, 47 Beaver Street, New York, or on loan from state cancer societies, state health departments and regional depots of Association Films, New York, Dallas, Chicago and San Francisco.

This motion picture was designed to promote earlier diagnosis of carcinoma of the breast. It effectively demonstrates the parts played by "physician suspicion," careful examination and reliance on surgical biopsy in arriving at an early specific diagnosis. There is a brief historical introduction. The statistics of mammary cancer are discussed in a manner adequate to make the average physician conscious of the fact that early cancer of the breast is clinically indistinguishable from a benign lesion. Essential facts in the embryologic and later developmental processes in the breasts are shown clearly in animation, as are the cyclic changes associated with menstruation, pregnancy and lactation. The production of cancerous lesions by the infiltrating type of growth is also shown by animation. The physical examination is illustrated in great detail, with emphasis on the elicitation of the earliest retraction signs. Methods of palpation and manipulation of the breasts in order to reveal conditions suggestive of carcinoma are amply illustrated. The need for gentle, thorough examination of both breasts, axillae and supraclavicular fossae is stressed. The importance of systematic follow-up examinations at specific intervals to discover possible recurrence and metastases is outlined. The most important lesson to be learned from this film is that early tumor discovery with biopsy diagnosis is the key to success in treatment of breast cancer.

This motion picture is highly recommended as a means of reemphasizing important facts about breast cancer for hospital staffs, medical societies and indeed for any physicians having the opportunity to examine breasts. It is well planned, well organized and carefully produced. The photography, animation and narration are excellent.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Necessity for Expert Testimony. — This was an action for damages allegedly due to the negligence of the defendant physician. From the denial of the defendant's motion for judgment, the defendant appealed to the court of appeals of Ohio, Cuyahoga County.

The plaintiffs, husband and wife, filed separate actions against the defendant physician for malpractice growing out of an operation performed by the defendant on the plaintiff wife. The operation was what is known to medical science as a total hysterectomy. After the operation had been performed and the plaintiff wife had been discharged from the hospital, she developed symptoms of burning, urging and incontinence. After an examination made by the defendant, the plaintiff wife was referred to a urologist, whose examination disclosed that the plaintiff wife's bladder was inflamed and infected. The urologist also found several "bladder stones." He testified, however, that he found no surgical damage to the bladder walls. The plaintiff wife's complaint of burning, urging and incontinence continued, and the urologist examined her again, with about the same result. A further examination a few days later, however, which was almost three months after the operation, disclosed a leak in the bladder known to medical science as a vesicovaginal fistula. This fistula was subsequently repaired by another physician.

After the defendant had finished the hysterectomy operation and the plaintiff had been returned to her room, a catheter was inserted into her bladder and a mixture of blood and urine was discharged, which discharge continued until a few days before she left the hospital. Both plaintiffs testified that when this fact was called to the attention of the defendant directly after the operation, he said, "I nipped her bladder." This was denied by the defendant. The plaintiffs' cases are based on their contention that the defendant was negligent in puncturing the bladder during the hysterectomy and in failing to repair such puncture after it had been made.

The burden of proving negligence and proximate cause in a malpractice case, said the court of appeals, is on the plaintiff and the fact that an injury has been suffered will not, without affirmative evidence tendered by the plaintiff as to the cause and effect of such injury, be presumed to have been the result of the doctor's negligence. By the great weight of authority, the court continued, when the physician's want of skill or lack of care in the treatment of a patient or in conducting a major operation is in question, expert medical testimony is necessary to establish the claimed negligence of the physician and that such negligence has some causal connection with the claimed injury. What is or is not standard practice and treatment in a particular case, or whether the conduct of the physician measures up to the standard, is a question for experts and can

be established only by their testimony. The only exception to this rule, the court said, is that where the want of skill or lack of care is so apparent as to be within the comprehension of laymen and requires only common knowledge and experience to understand and judge it expert evidence is not essential. Furthermore, the court of appeals said, there seems also to be unanimity in the cases that the plaintiff must establish that the claimed injuries were a probable result of the physician's negligence when established and not that such result was a mere possibility.

In a prior case emanating from the state of Washington, wherein the physician was charged with negligence in removing a uterus, it being claimed that he negligently cut the bladder during such operation, the court said: "All of the physicians who testified on both sides united in saying that in an operation such as this it is necessary to peel as close to the bladder as it is possible to do without injuring the walls of the bladder. . . . The consensus of all of the medical testimony on both sides of this case is that vesicovaginal fistula may follow a hysterectomy for cancer, and the fact that it does follow is no evidence of lack of skill in the performance of the operation."

From the record before us, said the court, we find no medical evidence relating to the nipping of the bladder as a probable cause of the burning, urgency and incontinence suffered by the plaintiff subsequent to her operation or that there was any causal connection between such claimed nipping and the vesicovaginal fistula which was subsequently found by the urologist. Nor is there any medical evidence to support the evidence of the plaintiffs that the defendant admitted nipping the plaintiff wife's bladder, which claim was completely denied by the defendant.

Accordingly the court concluded that it was the duty of the trial court to grant the defendant's motion for judgment and the judgment of the trial court was therefore reversed and final judgment entered in favor of the defendant physician.—*Modrzynski v. Lust (2 cases), 88 N. E. (2d) 76 (Ohio, 1949).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations. July 21. *Oral.* Philadelphia, April 23-27, Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Oral.* Washington, April 14-16. Sec., Dr. George M. Lewis, 66th Street, New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Boston, April 13-15. San Francisco, June 21-23. The oral examinations in the subspecialties will be held at the same time and places. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Oral Part II.* Atlantic City, May 21-28. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1951. Final date for filing applications is July 1, 1950. *Practical.* Boston, May 22-26; Chicago, Oct. 2-6; West Coast, Jan. 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* San Francisco, May. Chicago, October. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Madison, Wis., April 11-12. St. Louis, Nov. 10-11. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis.

AMERICAN BOARD OF PEDIATRICS: Philadelphia, March 31-April 2; Cincinnati, May 5-7; San Francisco, June 30-July 2. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Boston, Aug. 26-27. Final date for filing applications is April 1. Sec., Dr. Robert L. Bennett, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral.* May-June. Sec., Dr. Louis T. Byars, 4647 Pershing Avenue, St. Louis, Mo.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Spring Examination. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, week of June 18. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, Oct. 25. Final date for filing applications is July 1. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ARKANSAS: * *Examination.* Little Rock, June 8-9. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main Street, Little Rock.

CALIFORNIA: *Examination, Written.* San Francisco, June 19-22; Los Angeles, Aug. 21-24; Sacramento, Oct. 16-19. *Examination, Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 18; Los Angeles, Aug. 20; San Francisco, Nov. 12. *Reciprocity, Oral Examination.* San Francisco, June 17; Los Angeles, Aug. 19; San Francisco, Nov. 11. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

DELAWARE: *Examination.* Dover, July 11-13. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

FLORIDA: * Jacksonville, June 25-27. Sec., Dr. Frank D. Gray, 12 N. Rosalind Avenue, Orlando.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Endorsement.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

HAWAII: *Examination.* Honolulu, July 10-13. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 10. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: Chicago, April 4-6. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Iowa City, June 12-14. Sec., Dr. M. A. Royal, 506 Fleming Building, Des Moines 19.

KANSAS: Kansas City, June 7-8. Sec., Dr. J. F. Hassig, 905 N. 7th Street, Kansas City.

KENTUCKY: *Examination.* Louisville, June 14-16. Sec., Dr. Bruce Underwood, 620 S. 3rd Street, Louisville 2.

MARYLAND: *Examination.* Baltimore, June 20-23. Sec., Dr. Lewis P. Gundry, 1215 Cathedral Street, Baltimore 1, *Homeopathic.* Baltimore, June 20-21. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MISSOURI: *Reciprocity.* St. Louis, March 26. *Examination.* St. Louis, May 31-June 2 and June 7-9. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Building, St. Louis.

MONTANA: Helena, April 3-5. Sec., Dr. Otto G. Klein, First National Bank Building, Helena.

NEBRASKA: * *Examination.* Omaha, June 5-7. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Building, Lincoln 9.

NEVADA: Carson City, May 1. Sec., Dr. George H. Ross, 112 Curry Street, Carson City.

NEW JERSEY: *Examination.* Trenton, June 20-23. Sec., Dr. E. S. Hallinger, 28 West State Street, Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGoey, Coronado Building, Santa Fe.

NORTH CAROLINA: *Endorsement.* Pinehurst, May 1. *Written.* Raleigh, June 19-22. *Endorsement.* Raleigh, June 19. Sec., Dr. Ivan Procter, 226 Hillsboro Street, Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 5-7. *Reciprocity.* Grand Forks, July 8. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Reciprocity.* Columbus, April 3. *Examination.* Columbus, June 14-17. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: *Endorsement.* Portland, April 28-29. *Written.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Building, Portland 4.

RHODE ISLAND: * *Examination.* Providence, April 6-7. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 26-29. *Reciprocity.* First Monday of each month. Sec., Dr. N. B. Heyward, 1329 Blanding Street, Columbia.

SOUTH DAKOTA: * Sioux Falls, July 18-19. Sec., Dr. C. E. Sherwood, 300 First National Bank Bldg., Sioux Falls.

TEXAS: * *Examination.* Austin, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, June. Dir., Dr. Frank E. Lees, 324 State Capitol Building, Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 23-24. *Endorsement.* Richmond, June 22. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WEST VIRGINIA: Charleston, April 3-5. Sec., Dr. N. H. Dyer, State Capitol, Charleston.

WISCONSIN: * Milwaukee, July 11-13. Sec., Dr. C. A. Dawson, River Falls.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, March 21. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, May 9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Building, Little Rock.

DISTRICT OF COLUMBIA: Washington, April 17-18. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Building, Washington.

FLORIDA: *Examination.* June 3. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, April 11. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MINNESOTA: *Examination.* Minneapolis, April 4-5. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, May 2-3. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

SOUTH DAKOTA: Vermillion, June 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th Street, Yankton.

TEXAS: *Examination.* Austin, April 21-22. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.

WISCONSIN: Madison, April 1. Milwaukee, June 3. Sec., Prof. W. H. Barber, Ripon.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1939 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

19:999-1094 (Nov.) 1949

Not for Ourselves Alone: Presidential Address. O. A. Brines.—p. 999.
*Incidence of Post-Transfusion Serum Hepatitis. J. J. McGraw Jr., M. M. Strumia and E. Burns.—p. 1004.
*Coagulation Mechanism: With Specific Reference to Interpretation of Prothrombin Time and Consideration of Prothrombin Consumption Time. A. J. Quick.—p. 1016.
Effect of Ultrafiltration and Carbon Dioxide on Antithrombin Activity of Fresh and Stored Human Plasma. M. Stefanini.—p. 1024.
Survey of Accuracy of Rh Antibody Titrations in Several Hospital Laboratories. R. W. Marsters.—p. 1032.
Interstitial Cell Tumor of Testis: Report of 2 Cases. C. R. Reiners Jr. and R. C. Horn Jr.—p. 1039.

Post-Transfusion Hepatitis.—McGraw and co-workers surveyed the incidence of serum hepatitis following transfusions of blood and plasma at the Bryn Mawr Hospital, Pennsylvania, over a four year period beginning December 1943. Questionnaires were sent to 1,300 control patients and to 1,523 patients who had received transfusions of blood or plasma. Satisfactory responses were obtained from 1,000 controls and 936 transfused patients. Among the 1,000 controls were 2 patients (0.2 per cent) with "probable hepatitis," in whom jaundice developed in a six month period starting two weeks after transfusion and whose signs and symptoms could not be definitely attributed to disease other than acute or subacute hepatitis. Among the 936 transfused patients there were 12 (1.3 per cent) with "probable hepatitis" and 20 (2.2 per cent) with "possible hepatitis." All patients in whom jaundice developed in the study period were recognized as having "possible hepatitis" even though other associated lesions, such as common duct stones or carcinoma of the pancreas seemed more likely to be the cause of jaundice. Of 382 patients who received blood and no plasma, only 1 (0.3 per cent) had "probable hepatitis." These patients received a total of 3,723 transfusions of blood or plasma, an incidence of 1 case of "probable hepatitis" per 300 units of transfused blood or plasma. Of the 936 transfused patients, 528 received a total of 2,351 units of plasma, with or without whole blood. Ten of these 528 patients had "probable hepatitis," an incidence of 1 case of hepatitis for every 235 plasma transfusions. Results suggest that hepatitis may be transmitted by transfusion. Hepatitis is apparently a rare complication following transfusion of whole blood, but its incidence is significantly increased by the use of pooled plasma. The larger the pool of plasma, the greater the chance for transmission of hepatitis. All donors should be rejected who have had jaundice within two years. One should not use more than 8 to 12 donors per pool. Measures for virus sterilization may be instituted.

Coagulation Mechanism.—According to Quick, thrombin formation is the key factor in hemostasis. A normal prothrombin time is dependable evidence that the concentration of prothrombin is normal and that, therefore, the production of thrombin will also be normal, provided the supply of thromboplastin in the blood is adequate. The prothrombin time test measures the prothrombin activity but furnishes no information concerning the thromboplastin concentration in the plasma. The prothrombin consumption test was developed to determine the value of this latter agent. The method consists in allowing blood to coagulate in a test tube and determining after fixed periods of time how much prothrombin remains in the serum. If the prothrombin consumption is normal, it indicates that both the thrombocytes and the concentration of thromboplastinogen are normal. The clotting power of blood can be quantitatively appraised by these two tests. The prothrombin time measures dysfunctions of the prothrombin complex, while the prothrombin consumption test determines the amount of thromboplastin available in the blood. On this basis the common hemorrhagic diseases resulting from coagulation defects can be classified into two principal classes, the hypoprothrombinemias and the thromboplastin deficiencies. Thrombopenia and hemophilia are the principal diseases in which a lack of thromboplastin occurs.

American J. Digestive Diseases, Fort Wayne, Ind.

16:383-424 (Nov.) 1949

Increase in Peptic Ulcer of Aged. F. W. Mulsow.—p. 383.
Newer Concept of Arthritis and Treatment of Arthritic Pain and Deformity by Sympathetic Block at Sphenopalatine (Nasal) Ganglion and Use of Iron Salt of Adenylic Nucleotide: "Dynamics of Muscle Tonus" Part IV. S. L. Ruskin.—p. 386.
Rh Pseudoagglutinative Properties of Procaine Parotid Mucin. R. D. Barnard, G. A. Weitzner and G. B. Gordon.—p. 401.
Clinical and Roentgenologic Aspects of Esophageal Lesions in Scleroderma: Report of 6 Cases. A. M. Kaisch.—p. 405.
Encephalopathy of Hyperinsulinism. A. Altschul and S. K. Fineberg.—p. 413.

American Journal of Diseases of Children, Chicago

78:635-820 (Nov.) 1949

*Subdural Hematoma and Effusion in Infants: Review of 55 Cases. A. R. Elvidge and I. J. Jackson.—p. 635.
*Morphologic Characteristics and Antibiotic Resistance of Hemophilus Influenzae. G. E. Foley, H. Shwachman, M. McGarry and W. D. Winter Jr.—p. 659.
External Anorectal Prolapse in Children During War Years. B. M. Tordoir.—p. 671.
Prophylaxis of Whooping Cough. M. J. Fox and R. Snartemo.—p. 677.
Prothrombin Studies on Blood of Premature Infant and Value of Vitamin K Therapy. H. N. Sanford, M. Kostalik and B. Blackmore.—p. 686.
Heredity in Infantile Type of Gaucher's Disease: Report of Case. E. Stransky and D. F. Dauis-Lawas.—p. 694.
Cardiac Enlargement in Uncomplicated Mitral Insufficiency in Children. J. H. Miller and B. G. Wedum.—p. 703.
Epidermolysis Bullosa. A. Matheson and D. C. Rosner.—p. 708.
Agglutinating Substances for Homologous Coliform Organisms: Observations on Their Occurrence in Serum and Feces of Infants. E. F. Rabe and D. L. Lunphy.—p. 717.
Mandibular Growth Disturbance in Rheumatoid Arthritis of Childhood. M. B. Engel, J. Richmond and A. G. Brodie.—p. 728.
Nature of Infantile Convulsions. R. A. Shanks.—p. 673.

Subdural Hematoma and Effusion in Infants.—Elvidge and Jackson analyzed records of 55 infants with subdural effusion or hematoma. These included 10 with evidence of cranial birth trauma, as shown by skull fractures in 6 infants and tentorial tears in 3 others. The patients presented histories of difficult labor, instrumental delivery and symptoms continuing since birth. At the time of admission to the hospital their average age was 1 to 5 days. The second group of 26 patients presented only indirect but most suggestive evidence of an intracranial birth injury. These children were admitted to the hospital at ages ranging from 13 days to 14 months. In the third group of 9 patients the etiologic classification of subdural effusions followed a severe postnatal head injury. The fourth group of 10 patients was designated as unclassified because there was no history of a difficult labor, instrumental delivery, prematurity or postnatal head injury. Subdural puncture is the only method of making an accurate diagnosis. Pneumography offers the advantage of outlining the extent of the effusion and differentiating from other causes of hydrocephalus and seizures, while in the postoperative period it is helpful in determining whether the subdural space is obliterated. Surgical treatment consists of emptying the subdural space and removing the membranes. The acute subdural hematoma, as in the group with definite birth injuries, is best treated by aspiration, for no membrane is usually present at this early stage. The chronic subdural effusion is most satisfactorily treated by subdural tap, by trepanation for identification of membranes and, if their presence is confirmed, by their early removal. Since the membranes are apt to cover the whole hemisphere, a portion remaining over one pole will restrict its expansion and thereby increase the potentiality toward mental retardation. Attention to the fluid and protein balance in the management of these infants will aid greatly in reducing the operative mortality. The amount of protein and fluid lost in the subdural space may be 5 and 10 per cent, respectively, of the daily requirements of the infant.

The fact that this protein is no longer utilizable for bodily needs is one reason why these infants appear so pale and undernourished.

Hemophilus Influenzae: Antibiotic Resistance.—Foley and his associates say that for the past fifteen years Hemophilus influenzae ranked first as the cause of bacterial meningitis at the Boston Children's Hospital. During the six year period 1942 to 1947, of a total of 338 cases of bacterial meningitis 115, or 34 per cent, were due to H. influenzae. The seasonal variation of influenzal meningitis appears to be similar to the seasonal incidence of H. influenzae in the nose and throat. Sensitivities to penicillin and streptomycin as determined by test tube titration in a semisynthetic medium on forty-one strains of H. influenzae, type B, isolated from spinal fluid and on twenty-four respiratory strains of H. influenzae indicated that all strains were inhibited by 0.001 to 0.032 mg. of streptomycin per cubic centimeter. The majority of strains were inhibited by 0.004 mg. or less of streptomycin per cubic centimeter. Sensitivity to penicillin showed greater variation, ranging from 0.04 to more than 20 Oxford units per cubic centimeter. The majority of strains required 2.5 or more Oxford units of penicillin per cubic centimeter. There was no significant difference in antibiotic sensitivity between the spinal fluid and respiratory strains. A comparison of the antibiotic sensitivities of twenty-two strains of H. influenzae, type B, from spinal fluid indicated that there was little correlation in results obtained between the cup and tube titration technics used in this study. A comparison of the sensitivities in vivo in chick embryo and in vitro by tube titration of five strains of H. influenzae, type B, from spinal fluid indicated that the in vivo inhibiting dose of streptomycin was consistently less than the in vitro values. The in vivo inhibiting doses of penicillin were inconsistent; those for three strains were less and those for two strains were greater than the corresponding in vitro inhibiting doses. The antibiotic sensitivity of a given strain varies with the technic used for its determination. Such values are significant only as a basis for comparison with other strains tested by the same technic in the same laboratory and are not necessarily an indication of the clinical response to be expected.

American Journal of Physiology, Baltimore

159:195-408 (Nov.) 1949. **Partial Index**

Effects of Oxygen Deprivation upon Cochlear Potentials. E. G. Wever, M. Lawrence, R. W. Hemphill and C. B. Straut.—p. 199.
Site of Action in Central Nervous System of Bacterial Pyrogen. W. W. Chambers, H. Koenig, R. Koenig and W. F. Windle.—p. 209.
Influence of Estrogens on Acute X-Irradiation Syndrome. H. M. Patt, R. L. Straube, E. B. Tyree, M. N. Swift and D. E. Smith.—p. 269.
Relation of Food Intake to Growth-Depressing Action of Natural and Artificial Estrogens. J. Meites.—p. 281.
Effect of Severe Stress upon Thyroid Function. R. H. Williams, H. Jaffe and C. Kemp.—p. 291.
Metabolism of Dogs During Intoxication from Agenized White Wheat Flour. E. P. Monahan and G. G. Lalanne.—p. 298.
Enzyme Studies on Human Blood. V. Estimation of Prothrombin by Homologous-Isolation Method. G. Y. Shinowara.—p. 303.
Effect of Blood Platelets on Prothrombin Utilization of Dog and Human Plasmas. J. A. Buckwalter, W. B. Blythe and K. M. Brinkhous.—p. 316.
Evolution of Prothrombin Conversion Accelerator in Stored Human Plasma and Prothrombin Fractions. B. Alexander and G. Landwehr.—p. 322.
Liver Regeneration in Presence of Common Bile Duct Obstruction. C. C. Ferguson, C. S. Rogers and H. M. Vars.—p. 343.
Influence of Graded Arterial Pressure Decrement on Renal Clearance of Creatinine, P-Aminohippurate and Sodium. E. E. Selkurt, P. W. Hall and M. P. Spencer.—p. 369.
Changes Produced in Hematocrit Value, Hemoglobin and Plasma Volume by Repeated Artificial Pneumothorax. W. C. Grant.—p. 394.

American Journal of Psychiatry, New York

106:321-400 (Nov.) 1949. **Partial Index**

The Accident-Prone Automobile Driver: Study of Psychiatric and Social Background. W. A. Tillmann and G. E. Hobbs.—p. 321.
Family Environment of Schizophrenic Patients. R. W. Lidz and T. Lidz.—p. 332.
Dynamics of Psychotherapy: Eclectic Point of View. E. G. Billings.—p. 346.
Use of Electroshock Therapy in Treating Psychiatric Patients with Associated Pulmonary Tuberculosis. H. P. Close.—p. 352.
Psychiatry at the Crossroads. R. L. Jenkins.—p. 358.
Philosophy and Methodology in Training of 500 Psychiatric Residents. J. H. Masserman, A. O. Hecker, J. Pessin and B. E. Boothe.—p. 362.
Society of Alcoholics Anonymous. William W., Co-Founder.—p. 376.
Oriental Mental Hospitals. E. Berne.—p. 376.

American Journal of Public Health, New York

39:1395-1516 (Nov.) 1949. **Partial Index**

Public Health of Tomorrow. C. F. Wilinsky.—p. 1395.
Health of American Indians. F. T. Foard.—p. 1403.
Persistent Hazards in Home Accident Pattern. D. B. Armstrong and W. G. Cole.—p. 1434.
Preschool Diphtheria Immunization Status of New York State Community: Comparison of Physician Reporting with School Entrance Records as Sources of Basic Data. F. R. Freckleton.—p. 1439.
Use of Mice for Detection of Small Amounts of Toxin in Cultures of C. Diphtheriae. M. Beattie.—p. 1455.
Occurrence and Distribution of Types of C. Diphtheria: California, July 1, 1940-June 30, 1948. M. Beattie.—p. 1458.
*Use of Egg Embryos in Culture of Mycobacterium Tuberculosis. E. McNelly and W. A. Riddell.—p. 1463.

Egg Embryos in Culture of Mycobacterium Tuberculosis.—Studies reported by McNelly and Riddell indicate that the embryo culture method is fully as sensitive as the conventional egg slant cultures. This is true of both the chorioallantoic membrane and the yolk sac inoculations. Although the latter method is simpler, it suffers from the same defect as other liquid culture mediums, namely, that there is no colony or lesion that can be evaluated as to type. Larger inoculums into the yolk sac usually kill the embryo, but this seldom happens with membrane inoculations. These have the advantage that lesions are evident and capable of evaluation as to type. It is a convenient method for enrichment prior to animal inoculation.

American Practitioner, Philadelphia

4:119-180 (Nov.) 1949

Rosacea Complex, Including Its Ocular Component. E. P. Cawley and A. C. Curtis.—p. 119.
Persistent Urethral Discharge: Causes and Management Following Therapeutic Failures with Chemotherapeutic and Antibiotic Agents. S. Keesal.—p. 124.
Allergy in General Practice. L. H. Criep.—p. 131.
Emergency Psychotherapy in General Practice, Hysteria and Epilepsy. W. C. Hulse and L. Lowinger.—p. 135.
Toward Improvement of Child Health Services. J. P. Hubbard.—p. 142.
Hepatitis and Jaundice: Review of 119 Cases. W. B. Bean and M. Franklin.—p. 148.
Psychiatric Implications of the Climacteric. C. H. Barnacle.—p. 154.
Present Status of Tetanus Immunization. C. Wesselhoeft.—p. 159.
Clinical Application of Recent Advances in Gastro-Intestinal Physiology. G. E. Wakerlin.—p. 163.

American Review of Tuberculosis, New York

60:393-538 (Oct.) 1949. **Partial Index**

Resected Postthoracoplasty Lung: Clinico-Pathologic Correlation. W. A. Meissner, R. H. Overholt, N. J. Wilson and J. H. Walker.—p. 406.
Tumors of Mediastinum: Discussion of Diagnostic Procedure and Surgical Treatment Based on Experience with 44 Operated Cases. L. A. Brewer III and F. S. Dolley.—p. 419.
Urinary Excretion of Amino Acids. M. S. Dunn, M. N. Camien, S. Akawie and Others.—p. 439.
Studies of Food Intake and Requirements of Women with Active and Arrested Tuberculosis. W. D. Brewer, D. C. Cederquist, C. J. Stringer and M. A. Ohlson.—p. 455.
*Appraisal of Contribution of Mass Radiography in Discovery of Pulmonary Tuberculosis. C. Silverman.—p. 466.
Suitable Dose of Tuberculin for Single Test Tuberculin Testing. K.-Y. Liu, H.-C. Ku and P. T. Y. Ch'iu.—p. 483.
Disposition and Follow-Up of Pulmonary Tuberculosis: Study Based on Character and Extent of Lesion Seen on Initial Roentgenogram. H. H. Fellows, J. A. Evans and M. G. Stephens.—p. 487.
Miniature Chest Roentgenograms in Schools and Industries in San Antonio, Texas. P. A. Pamplona and W. F. Hamilton.—p. 501.

Appraisal of Mass Radiography.—Silverman feels that the experience of the Baltimore City Health Department with the application of mass radiography to some fifty groups of the population, constituting 48,175 apparently healthy persons, or about 5 per cent of the population, has revealed a net yield of tuberculosis cases which appears rather modest in relation to the effort expended. One of the primary objectives of mass roentgenographic examinations is to increase the proportion of cases discovered with the disease in the minimal stage. The net yield in this respect was disappointing. Of 1,468 cases of pulmonary tuberculosis which came to official attention during the year, only 202 were classified as of active minimal disease, and of this number approximately one fourth were discovered by the survey. In spite of considerable effort expended in mass sur-

veys, the proportion of new cases discovered with the disease in the active minimal stage was not materially increased. The effort to find population groups which were contributing greatly to the tuberculosis problem of the community was unsuccessful. The frequency of positive findings was surprisingly similar in all the adult groups surveyed. The only significant differences noted were the lower rates found in the school groups, largely composed of adolescents. Whether or not mass roentgenographic examinations of all kinds of groups of apparently healthy persons should be continued remains to be determined. One possible modification of policy is to concentrate this effort more completely on adult groups living and working in the poorer and more crowded sections of the city and especially to seek out adult Negro groups. It also remains to be determined whether, in a community where tuberculosis is a major problem, an intensification of the search for new cases among the household associates and social and occupational contacts of known open cases may not yield a greater return for effort expended.

Annals of Internal Medicine, Lancaster, Pa.

31:545-714 (Oct.) 1949

'Use of BAL (British Anti-Lewisite) in Treatment of Injurious Effects of Arsenic, Mercury and Other Metallic Poisons. W. T. Longcope and J. A. Luetscher Jr.—p. 545.
'Diversity of Gouty Arthritis and Its Complications. J. H. Talbott. —p. 555.
Electron Microscopy in Relation to Medical Sciences. S. Mudd.—p. 570.
Pharmacodynamics of Pulmonary Absorption in Man. I. Aerosol and Intratracheal Penicillin. E. A. Gaensler, J. F. Beakey and M. S. Segal.—p. 582.
'Heredity of Gout and Its Relationship to Familial Hyperuricemia. R. M. Stecher, A. H. Hersh and W. M. Solomon.—p. 595.
Use of Curare (D-Tubocurarine in Oil and Wax) in Treatment of Muscle Spasm in Rheumatic Disorders. H. M. Margolis and P. S. Caplan.—p. 615.
Evaluation of Radical Surgery for Carcinoma of Pancreas and Ampullary Region. A. O. Whipple.—p. 624.
Use of Mixtures of Protamine Zinc and Regular Insulin. R. G. Sprague.—p. 628.
Summary of Evidence Relating Life Situation and Emotional Response to Peptic Ulcer. S. Wolf.—p. 637.
Calcareous Pancreatitis. C. A. Domzalski Jr.—p. 650.
Survey of Actualities and Potentialities of Exfoliative Cytology in Cancer Diagnosis. G. N. Papanicolaou.—p. 661.

BAL (British Anti-Lewisite) in Treatment of Injurious Effects of Metallic Poisons.—When cases of arsenical dermatitis due to contact with adamsite or diphenylamine chlorarsine, which had resisted treatment, were sent to Longcope and Luetscher from an arsenal they applied a salve containing 5 per cent and 10 per cent BAL (2,3-dimercaptopropanol). The results were so satisfactory that they extended this treatment to cases of dermatitis complicating the arsenical therapy of syphilis. The results were very satisfactory. Often within forty-eight hours after the intramuscular injections were begun the erythema, edema and itching of the skin subsided, while the weeping vesiculitis became dryer. In the early stages scaling may set in, and in the more advanced cases exfoliation may increase. Occasionally recovery took place with surprising rapidity, but usually it was several days before healing of the skin was complete. Evidence that arsenic is extracted from the tissues by BAL was demonstrated by the increased urinary excretion of arsenic. BAL is effective in hemorrhagic encephalitis and possibly in blood dyscrasias. Patients with agranulocytosis were treated with it with no fatal results. The immediate use of BAL in accidental overdosage in antisyphilitic arsenical treatment was attended with success. Good results were reported in postarsphenamine thrombopenic purpura and in optic neuritis following the use of tryparsamide. Records of 61 patients who were treated with BAL for acute poisoning by mercury bichloride demonstrate conclusively that BAL is an effective antidote for bichloride of mercury when treatment can be instituted within the first few hours. BAL has also proved effective in the treatment of untoward complications of gold therapy. Experimental studies on lead poisoning, however, revealed that the toxic effects of lead may actually be increased by BAL. An increase in the urinary excretion of lead was noted, but beneficial effects on the symptoms of lead poisoning were not observed.

Gouty Arthritis and Its Complications.—Talbott presents observations on 8 patients with gout in whom the diagnosis was established by most of the following criteria: a family history of gout, typical acute attacks of joint distress, response to colchicine, evidence of osseous tophi by roentgen ray examination, elevation of serum uric acid above 6.0 mg. per hundred cubic centimeters, subcutaneous tophi with sodium urate crystals and renal disturbance. The first patient is now 37 years of age. At the age of 6 he had trouble with his hip, and, although at the time this was regarded as tuberculous in nature, in retrospect it appears that the joint trouble was most likely gout. By the time he was 21 he had several acute attacks per year, which subsided after colchicine therapy. At 37 the lower leg was amputated because it was devitalized. Hardly a joint in his body had escaped arthritis and infiltration with urates. The second case concerns a patient with gout, who died from renal insufficiency. The appearance of gout in a woman before menopause is another factor which makes this case noteworthy. The third patient died of uremia at the age of 43. He had had acute nephritis 10 years before his first attack of gout. Commenting on the fourth case, the author says that the association of gout and rheumatoid arthritis is an uncommon occurrence. The development of the two conditions in one patient is probably coincidental. The fifth case represents an instance of minimal gouty arthritis. Death was caused by a myocardial infarct. The sixth patient was first seen at the age of 62, complaining of acute arthritis in the right foot. At the age of 50 he passed some gravel in his urine. He had three more episodes of passing gravel in the following 10 years. The gravel showed a high content of uric acid. The level of this serum uric acid varied from 6.2 to 12.4 mg. per hundred cubic centimeters. The seventh patient had a mild case of gout. His joint symptoms were controlled with hourly doses of colchicine during acute symptoms and a few colchicine tablets per week in the symptom-free periods. In the eighth case, one foot became tender after minor trauma to the instep. The serum uric acid was 7.4 mg. per hundred cubic centimeters. The roentgenograms of the feet showed decalcification in the affected foot only and one osseous tophus. The patient was given colchicine, 0.5 mg. every hour; after he had received 12 doses gastrointestinal distress developed. When the last dose of colchicine had been ingested the pain in the foot had lessened considerably. The author stresses that in acute attacks 0.5 mg. of colchicine should be given every hour until onset of gastrointestinal distress. Ten to 14 doses are usually sufficient. Colchicine is then stopped and camphorated opium tincture is given. In the patients with frequent attacks of arthritis, 1 or 2 colchicine tablets each day is advised. Less severe cases may require but 1 or 2 tablets per week. A balanced diet with a liberal fluid intake seems to produce as satisfactory results in many patients as does rigid dieting.

Heredity of Gout and Its Relationship to Familial Hyperuricemia.—According to Stecher and his associates an abnormally high level of uric acid in the blood is one of the manifestations of faulty uric acid metabolism, which is characteristic of gout. In this study familial hyperuricemia is considered to have the same significance as clinical gout. The study is based on 248 serum uric acid determinations on 201 members of 44 gouty families as well as on 1,024 serum uric acid determinations on 961 patients examined routinely at a general hospital. A division between hyperuricemic and normal values was recognized clinically at 6.5 mg. per hundred cubic centimeters. The incidence of hyperuricemia in the relatives of gouty patients was found to be 18 per cent among 11 mothers, 17 per cent among 24 brothers, 21 per cent among 24 sisters and 15 per cent among 33 sons. Not a single daughter among 45 tested was found to have hyperuricemia. There was no correlation between age and hyperuricemia among male relatives of gouty patients, but a significant correlation was found among female relatives. Since no female relative in this series was affected below the age of 50, it seems possible that normal menstrual function inhibits hyperuricemia. The genetic peculiarities of hyperuricemia are such that in some families it resembles an autosomal recessive, whereas in others it is more like an auto-

somal dominant. These peculiarities are, however, satisfactorily explained if the gene involved is an autosomal dominant, which has a much lower penetrance in the female than in the male. A tentative estimate of the penetrance is about 84 per cent in the heterozygous male, about 12 per cent or less in the female.

Archives of Dermatology and Syphilology, Chicago

60:641-838 (Nov. [Part 1]) 1949

Histologic Changes in Sensory Nerves of Skin in Herpes Zoster. M. H. Ebert.—p. 641.
*Primary Irritants and Sensitizers Used in Fabrication of Footwear. L. E. Gaul and G. B. Underwood.—p. 649.
*Treatment of Syphilis with Penicillin Injection in Oil and Wax U. S. P.: Analysis of 153 Cases. J. E. Rauschkolb and H. N. Cole.—p. 676.
*Reinfection and Relapse After Treatment of Early Syphilis with Penicillin: Analysis of 137 Cases of "Infectious Failure" in Total Series of 1,105 Cases. A. G. Schoch and L. J. Alexander.—p. 690.
Eosinophilic Granulomas of Skin. E. A. Oliver, J. R. Webster, J. E. Ginsberg and H. S. Steinberg.—p. 701.
Radium in Treatment of Hemangioma. F. Ronchese.—p. 717.
Early Reactions Following Roentgen Ray Epilations. L. Zugerman. —p. 722.
Experimental Studies on Treatment of Human Torulosis. A. M. Kligman and F. D. Weidman.—p. 726.
Superficial Mycoses of Veterans: I. Survey of 1,000 Veterans with Service Diagnosis of Dermatomycosis. R. C. Burke and F. E. Bumgarner.—p. 742.
Pyostomatitis Vegetans: Report of 3 Cases. F. P. McCarthy.—p. 750.
Nonlipid Granular Cell Tumors. H. N. Cole and H. Lund.—p. 765.
Use of Repellents in Clinical Dermatology: General Principles. L. Goldman.—p. 777.

Primary Irritants and Sensitizers in Footwear.—Gaul and Underwood investigated 160 cases of dermatitis arising from footwear. These patients were asked to bring in their shoes. A total of 350 shoes were torn apart. These included all types found in infants', children's, women's and men's footwear. The authors list materials that produced positive reactions in patch tests. Inquiries were made from manufacturers and clinicians. Sock linings of shoes consist of variously colored, coated leather, canvas and a wide choice of impregnated, natural or synthetic materials. Toe boxes are laminated substances, such as asphalt-impregnated felts. Heel counters are leather or paper. Liberal amounts of adhesives secure the linings to the shoe uppers. The insoles are treated leather, impregnated fabrics and coated cloth or paper. Heel pads are usually a coated paper. Insole materials are cemented to the bottom fillers of the shoes. Thus, the feet are encased in a moisture-repellent environment. Water-proofed materials in contact with the feet cause the skin to become sticky, especially in hot weather. Imbibition of cutaneous secretions by the horny layer and possibly also the rete, because the upper third of the sweat glands is patent, promotes absorption of allergens by the pedal skin. Sweating is continuous on the palms and soles. Diverse mechanisms, such as environmental changes, constitutional types and psychic and emotional stimuli, affect the degree of wetting of the feet. The tendency for attacks to occur in hot, humid weather is readily apparent. Another factor is the role of tension and pressure in causing the cutaneous penetration of allergens. Shoes are held on the feet by straps and laces, usually with the skin under tension. The sole is a weight-bearing area of skin. These additional factors need evaluation. The adhesives in footwear suggest the presence of resins, which are known to have a high sensitizing index. Many of the chemicals used in processing hides to convert them into leather may cause dermatitis, and recently various antimildew and fungicidal chemicals have been added. The belief has been expressed that eczematous eruptions of the hands can occur secondary to an eczematous contact dermatitis of the feet due to eczematogenous allergens in footwear. Since fungicides to destroy the dermatophytes have failed both in the prevention and in the treatment of dermatitis pedis, the authors urge that dermatologists form a council to appraise the hygienic needs of the foot and evaluate materials used in the manufacture of footwear with reference to their irritating properties.

Penicillin in Oil and Wax in Treatment of Syphilis.—A series of 175 cases, comprising 160 patients with primary and secondary syphilis and 15 patients with early latent syphilis, were treated by Rauschkolb and Cole with penicillin injection in oil and wax. All were hospitalized in the Cleveland City Hospital and received identical schedules of therapy, consisting of 600,000 units of penicillin administered intramuscularly once a day for eight days, for a total dose of 4,800,000 units. The data obtained on 116 of these patients form the basis of this report. This group included 50 with primary, 57 with secondary and 9 with early latent syphilis. Thirty-six of the 116 patients had serologic relapses, persistent seropositive reactions or clinical relapses. Of those who had a relapse, 20 were recognized as having a clinical relapse; 11 as having persistent seropositive reactions and 5 as having a serorelapse. Since a total dose of 4,800,000 units of penicillin in white wax and oil permitted a relapse rate of over 30 per cent, the authors feel that supplementation of this treatment or increase in the dose may be desirable.

Relapse in Early Syphilis.—Schoch and Alexander use the term "infectious failure" (infectious relapse) to describe results in patients who, months or years after treatment with penicillin for early syphilis, exhibit dark field positive lesions morphologically typical of primary and/or secondary syphilis. In 1,105 patients with primary or secondary syphilis who were treated with penicillin 5 different treatment schedules were used. The periods of observation ranged from nine months to three and a half years. One hundred and thirty-seven of these patients later exhibited evidence of infectious relapse (infectious failure). For 80 of the 137 patients the diagnosis of reinfection was made, and for 57, infectious relapse. The over-all incidence of reinfection in this study was 7.24 per cent, and that of infectious relapse was 5.16 per cent. Infectious relapse occurred almost entirely during the first year after treatment and was rare during the second year. Reinfection was much more prevalent in patients originally treated for primary syphilis than in patients treated for secondary syphilis. The authors feel that any patient who presents clinical signs of infectious syphilis one year or more after penicillin treatment for early syphilis should be regarded as having a reinfection rather than an infectious relapse. The treatment of reinfection is more successful than the treatment of early syphilis in general. The diagnosis of reinfection is relatively simple, provided adequate subjective and objective data are available. The authors have particular reference to serologic titer curves and positive epidemiologic findings.

Archives of Internal Medicine, Chicago

84:667-844 (Nov.) 1949

*Role of Blood Platelets in Thromboembolism. S. E. Moolten, L. Vroman, G. M. S. Vroman and B. Goodman.—p. 667.
Concepts of Myocardial Ischemia. H. H. Hecht.—p. 711.
Excretion of Choline in Urine of Diabetic Patients. T. Z. Csáky, J. Möllerström and O. V. Širek.—p. 730.
Multiple Hemorrhagic Sarcoma and Diabetes Mellitus: Review of Series, with Report of 2 Cases. W. B. Hurlbut and C. S. Lincoln Jr.—p. 738.
Clinical Manifestations of Carrión's Disease. W. E. Ricketts.—p. 751.
Hepatitis and Its Sequelae, Including Development of Portal Cirrhosis: Observations on 100 Cases. M. F. Koszalka, M. C. F. Linderl, H. M. Snodgrass and H. B. Lerner.—p. 782.
Defect of Ventricular Septum: Summary of 12 Cases and Review of Literature. A. Selzer.—p. 798.
Phytobezoar in Gastric Stump: Report of Case and Discussion of Therapy. L. Walk.—p. 824.

Role of Thrombocytes in Thromboembolism.—Moolten and his associates stress that the massing of thrombocytes as an adherent plug is the primary event in thrombosis. Clotting is its sequel and rapidly follows lysis of the accumulated thrombocytes, wherein clot-accelerating factors are liberated. The thrombocyte plug (white thrombus) is the principal means of attachment of the blood clot (red thrombus) until the latter is organized by invading fibroblasts. Clot retardation before organization favors the detachment of emboli. Endothelial "wettability" and thrombocytic adhesiveness are the principal governing factors in thrombosis. Experiments are described demonstrating relative nonwettability in unopened blood vessels and the progressive development of wettability under conditions which probably favor thrombosis. Analogous conditions probably exist in arteries damaged by atheroma, prolonged spasm or compression, in veins subjected to angulation, compression or inflammation and on the intravenous introduction of fat solvents such as ether and alcohol or of detergent agents, including the saponins of crude digitalis. Endocardial vegeta-

tions and mural thrombi in the heart may be similarly caused. An increase in the number and adhesiveness of thrombocytes results from the action of thrombocytosin, a lipid of body fat, which is probably liberated by direct trauma (surgical incisions, fractures, cutaneous irritations or cellulitis), by proteolytic or lipolytic ferments activated by tissue breakdown of any type (myocardial infarction, vascular gangrene or carcinoma) or after the ingestion of dietary fat. Thrombocytopen, a lipid of the spleen which suppresses thrombocyte formation and adhesiveness, is probably the antagonist of thrombocytosin. A new method of measuring thrombocytic adhesiveness to wettable surfaces is described: citrated blood is filtered through a wick of glass wool; the relative loss of thrombocytes by absorption is computed as the "adhesive index." A considerable increase in thrombocytic adhesiveness suggests a predisposition to thrombosis, whereas a decrease in adhesiveness is found in purpura associated with splenic hyperfunction. Thrombocytic adhesiveness is particularly high in cancer, paralleling an increased tendency to thrombosis. Similar observations occur in polycythemia vera, idiopathic thrombocythemia and related conditions. A rapid fall in the thrombocyte count, and particularly in the number of adhesive thrombocytes, from a previously high level often portends the formation of thrombi. Increased coagulability of blood is probably secondary to accelerated production of thrombin about white thrombi. Heparin sodium lowers thrombocytic adhesiveness and probably retards lysis. Thrombocytopen causes a fall in the thrombocyte count and adhesiveness and some prolongation of bleeding time; these effects suggest its value in the prophylaxis of thrombosis. Thrombocytosin, its antagonist, has been found useful in purpura. Deficient splenic function may be one of the factors which predispose to thrombosis. Conversely, normal splenic function may include protection of the circulatory tree against thrombosis.

Archives of Otolaryngology, Chicago

50:513-686 (Nov.) 1949

Surgical Treatment of Malignant Tumors of Inferior Alveolus and Mandible. J. J. Conley and G. T. Pack.—p. 513.
Surgical Correction of Abnormally Protruding Ear. O. J. Becker. —p. 541.
Anesthesia in Peroral Endoscopy, Especially General Anesthesia in Esophagoscopy and Gastroscopy. W. E. Pembleton and P. P. Vinson. —p. 561.
Ménière's Syndrome; Observations on Vitamin Deficiency as Causative Factor: II. Cochlear Disturbance. M. Atkinson.—p. 564.
*Acute Deafness in Scarlatina. H. Brunner.—p. 589.
Unilateral Paralysis of Larynx. W. C. Callaghan.—p. 605.
Idiopathic Paralysis of Vocal Cord: Fixation of Vocal Cord Without Anatomic Lesion. E. Glas.—p. 612.
Hydrogen Ion Concentration of Nasal Secretion in Situ in Newborn Infants. N. D. Fabricant and M. A. Perlstein.—p. 616.
Osteoma of Frontal Sinus. A. J. Vadala and K. Somers.—p. 618.
New Intralaryngeal Approach in Arytenoidectomy in Bilateral Abductor Paralysis of Vocal Cords: Report of Three Cases. W. C. Thornell.—p. 634.
Anterior Ethmoidal Nerve Syndrome: Referred Pain and Headache from Lateral Nasal Wall. H. H. Burnham.—p. 640.
*Chordoma of Maxillary Antrum and Nares: Report of Case Clinically Resembling Hodgkin's Disease First Diagnosed by Biopsy of Cervical Node. P. N. Pastore, P. F. Sahyoun and F. B. Mandeville.—p. 647.
Dental Considerations in Fitting Hearing Aid Ear Inserts. J. R. Anderson, W. Manion and A. C. Cota.—p. 659.

Deafness in Scarlatina.—Brunner reports a case of acute deafness associated with scarlatina and nasal diphtheria in a girl aged 14. Slight pain in both mastoid regions occurred on the second day after the appearance of the scarlatinal rash. A paracentesis performed on both sides was followed immediately by bilateral diminution of hearing, which within four days increased to complete deafness on both sides. Labyrinthine symptoms, such as dizziness and spontaneous nystagmus, were absent. The caloric reaction was diminished on both sides but was not absent. This elicitation of the caloric reaction suggested the diagnosis of serous labyrinthitis, because in purulent labyrinthitis the caloric reaction cannot be elicited. The diagnosis was confirmed by microscopic examination. The author's case proves that acute deafness in scarlet fever may be caused by bilateral otitis media plus bilateral diffuse serous labyrinthitis. The otitis media which caused the serous labyrinthitis was of the common and not of the necrotic type. The serous labyrinthitis which caused the deafness was characterized by an accumulation of a serofibrinous exudate in the endolymphatic and perilymphatic spaces. This exudate is carried away from the internal ear by phagocytes. Resorption of inflammatory products takes place in the endolymphatic duct. The serous labyrinthitis was caused by the passage of toxins through the intact windows. It caused deafness but failed to produce spontaneous labyrinthine symptoms. Serous labyrinthitis per se may cause not only transitory deafness but also permanent diminution of hearing. Hearing was not restored during the five and one-half weeks of illness preceding death. Necropsy revealed only moderate atrophy of the ganglion of the basilar portion, and nothing had occurred to indicate an organization of the exudate. These observations render it likely that hearing would have been restored had the child survived, though probably not to a normal extent.

Chordoma of Antrum.—Pastore and co-workers report a case of chordoma of the maxillary antrum and nares in a woman aged 32. The clinical picture resembled that of Hodgkin's disease, which was first diagnosed, based on biopsy of a cervical lymph node. The microscopic picture makes it obvious that a review of the histogenesis of chordoma is indispensable for differential diagnosis. The tumor has many of the morphologic characteristics of cartilage, while it expands, infiltrates and even metastasizes like carcinoma. The tumor cells in certain instances may be large, with clear cytoplasm and distinct cell membranes, and surrounded by hyaline and/or mucinous material and may suggest the diagnosis of chondroma. Other areas may show sheets of pavement cells, the most central of which are large and vacuolated. Some of the nests may be surrounded by hyaline bands. Mitotic figures are usually rare. This is the type which simulates carcinoma. When chordoma of this type invades a lymphoid structure, as the nasopharynx or the cervical lymph nodes, the resulting picture may simulate a lymphoepithelioma or even Hodgkin's sarcoma. The differential diagnosis depends on the observation of the physaliferous cells and the vacuolated cells, as well as the paucity of mitotic figures, and clinically on its slow course and precarious response to irradiation therapy.

Archives of Pathology, Chicago

48:491-612 (Dec.) 1949

*Bronchial Carcinoma: Practical Method of Early Diagnosis. K. R. Cross, T. E. Corcoran, T. J. Cooper and S. N. Landis.—p. 491.
Acclimatization Response and Pathologic Changes in Rats at Altitude of 25,000 Feet. B. Highman and P. D. Altland.—p. 503.
*Extragenital Choriocarcinoma with Comments on Male Origin of Trophoblastic Tissues. E. F. Hirsch.—p. 516.
Acute Closed Cerebral Lesions Treated by Injection of Hypertonic Dextrose Solution and by Surgical Decompression: Quantitative Study. C. B. Taylor, G. M. Hass and J. E. Maloney.—p. 525.
Effects of Prolonged Administration of Antithyroid Compounds on Thyroid and Other Endocrine Organs of the Rat. J. Seifter, W. E. Ehrich and G. M. Hudyma.—p. 536.
Bilateral Extensive Focal Ischemic Atrophy of Kidneys. H. W. Christofersen and E. F. Hirsch.—p. 548.
Influence of Age on Mammary Growth and Involution in Male Mice Treated with Estrogen. R. Silberberg and M. Silberberg.—p. 557.
Gastric Paraganglioma with Ulceration: Report of Case. C. K. Jones and F. W. McKee.—p. 570.
Normal Occurrence of Histologically Demonstrable Fat in Liver of the Newborn Infant. J. R. Dorkin and T. Weinberg.—p. 578.
Degenerative Renal Lesions Induced by Prolonged Choline Deficiency. J. J. Lalich, B. E. Kline and H. P. Rusch.—p. 583.

Diagnosis of Bronchial Carcinoma.—Cross and co-workers report a bronchoscopic study of 81 patients in whom carcinoma of the lung was suspected. Aspirated material and/or washings were obtained during a period of twenty-seven months. Twenty-four of the 81 patients were proved to have bronchial carcinoma by biopsy of the primary lesion, surgical resection of pulmonary tissues for biopsy, necropsy, or roentgenologic and clinical criteria acceptable to all departments concerned as diagnostic of bronchogenic carcinoma. Of the 24 proved cases of bronchogenic carcinoma, bronchial washings were suggestive but not diagnostic in 2, strongly suggestive in 3 and diagnostic in 10. The diagnosis of cancer was not reported in 9 cases. In 9 of the last 10 patients examined, bronchial carcinoma was positively diagnosed by aspirated material and/or washings obtained through the bronchoscope. This method constitutes a valuable source of cancer cells, particularly as cell groups, for the diagnosis of bronchogenic carcinoma. The material, after

centrifugation, can be fixed, embedded, sectioned and stained just as any other biopsy material. Examination of aspirated bronchial material and/or washings constitutes an aid to the early diagnosis of bronchogenic carcinoma of such great value that its use can no longer be ignored by the general pathologist.

Extragenital Choriocarcinoma.—Hirsch reports a case of primary choriocarcinoma of the right perinephric retroperitoneal tissue in a man aged 26. Choriocarcinoma, originally regarded as cancer of the trophoblastic tissues of the placenta, occurs also, in many instances, in the testis of fully mature males and, in a few instances, in the ovary of young or adolescent females. In a small number of cases it occurs in extragenital tissues, usually retroperitoneal or mediastinal, but in these cases exclusively in fully mature male patients. Chorionic gonadotropin, the active principle of the Aschheim-Zondek reaction, appears in the urine of patients with choriocarcinoma and provides biologic evidence, in addition to the tissue structure, that the tumor confains trophoblastic elements. The process of fertilization, parthenogenetic or hermaphroditic, seemed convenient to use theoretically for the explanation of these tumors, probably because choriocarcinoma was recognized as a cancerous complication of pregnancy. Trophoblastic tissues theoretically may be derived from potential elements of either the sperm or the ovum, not necessarily from the composite tissues produced by the fusion of the two. Fertilization, accordingly, simply provides conditions favorable for the growth of choriocarcinoma. Trophoblastic tissues are a characteristic of mature male germinal tissues (testis), not of the mature female (ovary), and the male element contributes the trophoblastic tissue component when choriocarcinoma develops in the uterus or adnexa as a complication of pregnancy. This could also imply that the testicular choriocarcinoma provides evidence that the trophoblastic tissues (placenta) are contributed by the male element in the normal development of a fertilized ovum in the uterus.

Arkansas Medical Society Journal, Fort Smith

46:93-108 (Oct.) 1949

Pathogenesis, Diagnosis and Management of Acute Poliomyelitis. E. S. Miller.—p. 93.

46:109-122 (Nov.) 1949

Coronary Artery Disease. J. W. Verser.—p. 109.
Care of Poliomyelitis at Local Level. W. A. Reilly.—p. 111.

Blood, New York

4:1183-1280 (Nov.) 1949

Diagnosis and Mechanism of Hemolysis in Chronic Hemolytic Anemia with Nocturnal Hemoglobinuria. J. V. Dacie.—p. 1183.
*Acquired Hemolytic Anemia: I. Relation of Erythrocyte Antibody Production to Activity of Disease. II. Significance of Thrombocytopenia and Leukopenia. R. S. Evans and R. T. Duane.—p. 1196.
Serologic Method of Purifying Blood Group A Substance. W. C. Boyd and R. M. Reguera.—p. 1214.
Hemolytic Reactions Produced in Dogs by Transfusion of Incompatible Dog Blood and Plasma: I. Serologic and Hematologic Aspects. L. E. Young, D. M. Ervin and C. L. Yuile.—p. 1218.
Id.: II. Renal Aspects Following Whole Blood Transfusions. C. L. Yuile, T. F. Van Zandt, D. M. Ervin and L. E. Young.—p. 1232.
Effects of Intramuscular Administration of BAL (2,3 Dimercaptopropanol) in Subject with Sickle Cell Trait: Case Report. W. J. Kuhns.—p. 1240.
Rh Isosensitization in the American Negro. M. S. Sacks, J. A. Guilbeau Jr., G. T. Bradford and E. F. Jahn.—p. 1245.
Pathogenesis of Erythroblastosis Fetalis. B. S. Kline.—p. 1249.
Correlation Between Mean Corpuscular Volume and Reticulocytosis in Phenylhydrazine Anemia in Swine. F. D. Lawrason, D. C. Eltzholtz, C. R. Sipe and P. K. Schork.—p. 1256.
Fetal and Adult Hemoglobins in Blood of Infants Affected with Hemolytic Disease of the Newborn. E. Ponder and P. Levine.—p. 1264.
Coincidence of Mediterranean Anemia and Pernicious Anemia in Young Sicilian. W. H. Crosby and H. J. Sacks.—p. 1267.

Acquired Hemolytic Anemia.—Evans and Duane report observations on 11 patients with acquired hemolytic anemia. The patients exhibited evidence of sensitization of their erythrocytes by an antibody-like agent in contrast to patients with congenital hemolytic jaundice. Abnormal destruction of transfused cells in vivo was demonstrated in all 9 patients in whom data were obtained on the longevity of transfused cells. The sensitizing agent was found to be adsorbed on the erythrocytes when it could not be demonstrated in the serum. A rough method of assay of the amount adsorbed was devised by making serial dilutions of the anti-human serum rabbit serum (antiglobulin serum) which was employed for the agglutination tests. With this technic a fairly consistent correlation was observed between the amount of antibody on the cell and the activity of the disease. Splenectomy when successful appears to exert a curative effect by sharply reducing the amount of antibody substance on the cell. Patients who had not responded to splenectomy in the past showed evidence of saturation of their cells with adsorbed antibody. The erythrocytes of patients who had responded to splenectomy and were in remission when studied showed distinctly less antibody on the cell by the same technic. Two patients entered spontaneous remissions after a long period of activity. The onset of remission in both was associated with a decrease in the amount of adsorbed immune antibody. One patient showed evidence of return of antibody production without immediate recurrence of the hemolytic anemia. This inconsistency is not explained. The tendency toward spherocytosis as measured by increased osmotic fragility may or may not be present in acquired hemolytic anemia. The most decided increase in hypotonic fragility was observed in the patient whose disease was most active prior to splenectomy. Continued activity of the disease after splenectomy was productive of the most extreme increases in spherocytosis. This suggests that the spherocytic cells are removed from the circulation by the spleen. Agglutination of red cells when the amount of adsorbed antibody reaches a critical level, together with such other phenomena as stasis, spherocytosis, increased mechanical fragility and possibly phagocytosis, probably explain the increased destruction of cells. Five of the 11 patients had thrombopenia, and 2 of the 5 had a pronounced degree of leukopenia along with active hemolytic anemia. Only 1 of these 5 patients had clinical manifestations of purpura. Abnormal immune mechanisms could account for both excessive destruction and deficient formation of thrombocytes.

Bulletin New York Academy of Medicine, New York

25:671-746 (Nov.) 1949

General View of Cancer Research. L. A. Scheele.—p. 671.
Evaluation of Surgical Treatment of Hypertension. R. H. Smithwick.—p. 698.
Recent Advances in Therapy of More Common Protozoan and Helminthic Infections of Man. H. Most.—p. 717.

25:747-804 (Dec.) 1949

Advances in Diagnostic Methods. B. P. Watson.—p. 747.
Diagnostic Significance of Electrolyte Disturbances. J. P. Peters.—p. 749.
Present Status of Clinical Electroencephalography. F. A. Gibbs.—p. 764.
Chronicle of One Hundred Years of Otolaryngology. A. C. Furstenberg.—p. 775.
Chemistry of Chloromycetin. H. M. Crooks Jr.—p. 792.
Clinical Use of Synthetic and Fermentation Chloramphenicol (Chloromycetin). J. E. Smadel.—p. 794.
Clinical Use of Chloramphenicol (Chloromycetin) in Certain Bacterial Infections. T. E. Woodward.—p. 795.

California Medicine, San Francisco

71:319-384 (Nov.) 1949

Chemotherapy in Viral and Rickettsial Disease. G. Meiklejohn.—p. 319.
Acute Coronary Thrombosis. G. E. Burch.—p. 322.
*Difficulties in Evaluating Systolic Murmurs in Children with Special Reference to Functional Systolic Murmur. M. B. Harrison.—p. 325.
Carcinoma of Rectum: Low Abdominal Transverse Incision for Resection with End-to-End Anastomosis. L. S. Cherney.—p. 329.
Study of Inflation of Lungs of Newborn: Preliminary Report. A. C. Hilding.—p. 332.
Interdependent Superiority and Inferiority Feelings. H. V. Ingham.—p. 337.
Tonsillectomy in Allergic Child. B. F. Feingold.—p. 341.
Physiology and Management of Climacteric. G. F. Jones.—p. 345.
Non-Allergic Wheeze. A. Goldman.—p. 349.
Consideration of Some Factors Causing Death in Operating Room. J. B. Dillon.—p. 353.

Systolic Murmurs in Children.—Harrison says that in the interpretation of cardiac murmurs in children the pendulum has swung from one end of the arc, where all systolic murmurs were considered indications of heart disease, to the other end, where practically none of the systolic murmurs were considered indicative of heart disease. Somewhere between these two points of view lies the real answer. This review is based on observations in the Children's Cardiac Diagnostic Clinic of the

San Francisco Health Department. As a guide in distinguishing between organic and functional systolic murmurs, five characteristics of a murmur should be noted: (*a*) the location of maximal intensity of the murmur; (*b*) the intensity of the murmur itself; (*c*) the character of the murmur (blowing, rumbling, rough or harsh); (*d*) the transmission of the murmur, and (*e*) the duration of the murmur and its time within the cardiac cycle. Functional systolic murmurs may be found at any of the valve areas; they usually are: faint to moderately loud; soft and blowing in quality; only slightly transmitted, and not heard immediately after the first heart sound. In doubtful cases, those in which history and physical examination alone are not sufficient to make a diagnosis of functional systolic murmur, further studies should be undertaken to determine the presence or absence of organic heart disease. Until a diagnosis of organic heart disease can be made with reasonable certainty, there should be no restriction of the activity of the patient, so as not to favor the development of a cardiac neurosis.

Canadian J. of Research. Medical Sciences, Ottawa

27:245-308 (Oct.) 1949. **Partial Index**

*Effect of Liver Extract Preparation on Bone Marrow Explants. K. E. Armbrust and H. D. Bett.—p. 245.
Electron Microscopy of Typhus Rickettsiae. C. E. Van Rooyen and G. D. Scott.—p. 250.
Detection and Assay of Hyaluronidase by Means of Mucoid Streptococci. R. G. E. Murray and R. H. Pearce.—p. 254.
Microcolorimetric Determination of Inorganic Phosphate in Plasma and Urine: I. Quantitative Investigation of Present Common Procedures; II. Sensitive and Stable Method for Plasma, Serum, and Urine. J. R. Polley.—p. 265.

Effect of Liver Extracts on Bone Marrow Explants.—Armbrust and Bett studied the effect of various concentrations of several liver extract preparations on the migration of cells, chiefly leukocytes, from explants of guinea pig bone marrow. The migration has been shown to be stimulated by an extract of liver, which shows incomplete activity in the treatment of pernicious anemia. Two clinically active fractions have been shown to be inactive in the stimulation of cell migration. The authors conclude that the migration of cells from explants cannot be used as a test for antipernicious anemia activity of liver extract preparations.

Cancer Research, Chicago

9:639-700 (Nov.) 1949. **Partial Index**

Factors Affecting Distribution of Tumor Metastases: Experiments with V2 Carcinoma of Rabbits. D. R. Coman, R. B. Eisenberg and M. McCutcheon.—p. 649.
Carcinogenic Activities of Certain Halogen Derivatives of 4-Dimethylaminoazabenzene in Rat. J. A. Miller, R. W. Sapp and E. C. Miller.—p. 652.
Electrophoretic, Nitrogen, Lipide and Enzyme Studies of Plasma and Plasma Fractions in Cancer. G. H. L. Dillard, H. R. Pearsall and A. Chanutin.—p. 661.
Correlation of Fluorescence of Human Urine with Benign and Malignant Growth. H. M. Rabinowitz.—p. 672.
Distribution and Action of Radioactive Oxazine Dye in Tumor-Bearing Mice. H. A. Sloviter.—p. 677.
Evaluation of Diagnostic Tests for Cancer: II. Inhibition of Serum Alkaline Phosphatase by Zinc Ion (Roche Test). W. H. Fishman, A. Wayne and F. Homburger.—p. 681.
Influence of Thyroid Hormone on Formation of Induced Skin Tumors in Mice. H. Silverstone and A. Tannenbaum.—p. 684.
Vitamin B_6 and Biotin in Human Cancer Tissue. R. M. Ballantyne and E. W. McHenry.—p. 689.

Florida Medical Association Journal, Jacksonville

36:257-332 (Nov.) 1949

*Master Two Step Exercise Test in Diagnosis of Coronary Insufficiency. K. B. Hanson.—p. 275.
Diagnosis of Commoner Hemorrhagic Diseases. J. N. Patterson.—p. 280.
General Allergies in Children. C. C. Maguire.—p. 287.
Clinical Response to Crowe's Vaccine in 125 Cases of Rheumatic Disease. K. Phillips.—p. 290.

Master Two Step Exercise Test in Coronary Insufficiency.—A standardization exercise test, with employment of the Master two step technic, was used by Hanson on 65 patients, all but 1 of whom had some type of chest complaint suggestive of heart disease. In 25 there was a positive result. Only 6 had changes in the control electrocardiograms compatible with coronary disease before the test. This type of exercise test makes it possible to obtain objective evidence of coronary insufficiency in a much higher percentage of patients with disease of the coronary arteries or other heart disease. The test is of value chiefly when the response is positive. When a double test gives negative results, it might be inferred that at the moment relatively good coronary reserve exists. The test is safe.

Georgia Medical Association Journal, Atlanta

38:423-476 (Oct.) 1949

Clinical Significance of Closure of Retinal Vessels. W. L. Benedict.—p. 423.
*Epileptic Variants Often Mistaken for Psychoneuroses: Differential Diagnosis and Treatment. R. W. Graves.—p. 433.
Emotional Aspects of Physical Disease. R. Chalmers and L. F. Woolley.—p. 436.
Fracture Problems of Lower Extremity. T. P. Goodwyn.—p. 443.
Technic for Vaginal Hysterectomy with Only Four Vascular Pedicles with Aid of Special Cystic Duct Hemostatic Forceps. C. Thompson.—p. 452.
Polycythemia Vera. J. C. Norris.—p. 459.

Epileptic Variants Mistaken for Psychoneuroses.—Graves says that, whereas the two most common symptoms of epilepsy, the major convulsive seizure and the petit mal blank spell, are readily recognized, there are epileptic variants which are not so well known. He describes two instances of myoclonic epilepsy, one in a mechanic who was accused of being an irresponsible prankster because almost daily his wrench would suddenly fly out of his hand. This man also recalled that occasionally, while combing his hair, the comb would be propelled from his hand. There were two instances when his right leg had suddenly jerked out from under him. These coordinated muscular jerks were entirely involuntary. In this case as well as in the case of a girl who was accused of throwing dishes, the epileptic misdemeanors were prevented with diphenylhydantoin sodium. Narcoleptic seizures may be associated with strange attacks of the subjects suddenly becoming limp all over and, if standing, sinking to the ground. These seizures are called cataplexy, and the limpness is due to sudden loss of muscular tonus. Epileptic discharges from the autonomic centers in the hypothalamus may cause sudden dilatation of the pupils, flushing of the face, gooseflesh, tachycardia and tremulousness. Such autonomic seizures are usually mistaken for anxiety attacks. Psychomotor variants include lapse of memory, temper tantrums, disorientation in space or time, feelings of strangeness during which persons and places seem unfamiliar and the so-called dreamy states of the uncinate syndrome. Knowledge of four characteristics common to most epileptic seizures will greatly assist with the diagnosis: (1) The attacks are episodic in nature, (2) the beginning and termination of each episode are well defined, (3) each seizure tends to follow the same pattern and (4) the attacks are usually unmotivated and unrelated to environmental factors. It is not unusual for these variants to be succeeded sooner or later by generalized fits. Careful study is essential before one labels the seizures as "idiopathic," because any of the epileptic variants may result from such serious conditions as a brain neoplasm or a degenerative disease of the nervous system. It is important that patients with epileptic variants receive proper treatment. It is also important that both the perplexed patient and puzzled family be given an adequate explanation.

Industrial Medicine and Surgery, Chicago

18:451-492 (Nov.) 1949. **Partial Index**

Conservative Treatment of Industrial Intervertebral Disc Injuries. E. Loopesko.—p. 457.
*Employment of Hypertensives in Industry. E. W. Probst.—p. 462.
Injury vs. Gout. J. E. Kirkpatrick.—p. 464.
Sickness Disability Insurance Laws in Relation to Occupational Medicine. L. J. Goldwater.—p. 473.
Graphite (Plumbago, Black Lead) as Source of Dusty Lung Disease. C. P. McCord.—p. 483.
Intravenous Procaine as Outpatient Procedure. L. Cozen.—p. 487.

Employment of Patients with Hypertension.—In comparing the industrial performance and accident records of 89 hypertensive persons with those of an equal number of persons who did similar work but did not have hypertension, Probst found that the incidence of accidents in this small group of persons with hypertension was significantly less than in the

group without hypertension. This observation, in conjunction with cited previous studies and the opinions of leading cardiologists, indicates that persons with hypertension are good industrial risks and that many persons with blood pressures above the usual arbitrary normal limits can serve industry satisfactorily over long periods. It is suggested that the so-called normal blood pressure levels for preemployment industrial examinations be revised upward.

Journal of Bone and Joint Surgery, Boston

31-A:693-950 (Oct.) 1949. **Partial Index**

*Influence of Contact-Compression Factor on Osteogenesis in Surgical Fractures. G. W. N. Eggers, T. O. Shindler and C. M. Pomerat. —p. 693.
Trumble Operation for Fusion of Hip. G. W. Van Gorder.—p. 717.
Technique for Arthrodesis of Hip Joint. A. DeF. Smith and O. D. Babb.—p. 727.
Slipping of Upper Femoral Epiphysis. M. B. Howorth.—p. 734.
Fractures of Both Bones of Forearm in Adults. R. A. Knight and G. D. Purvis.—p. 755.
Experiences in Use of Homogenous (Bone Bank) Bone. J. B. Weaver. —p. 778.
Clinical Evaluation of Merthiolate Bone Bank: Preliminary Report. F. C. Reynolds and D. R. Oliver.—p. 792.
Causes for Amputations Performed at Walter Reed General Hospital During 1947 and 1948. A. W. Spittler and L. W. Taylor.—p. 800.
*Early Effects of Partial Sensory Denervation of Hip for Relief of Pain in Chronic Arthritis. B. E. Obletz, L. M. Lockie, E. Milch and I. Hyman.—p. 805.
Obturator Neurectomy for Coxalgia: Anatomical Study of Obturator and Accessory Obturator Nerves. R. A. Kaiser.—p. 815.
Procaine Injection for Relief of Pain in Hip. W. V. Ergenbright and F. C. Lowry.—p. 820.
Electromyography in Orthopaedica. A. L. Watkins.—p. 822.
Use of Technique of Progressive-Resistance Exercise in Adolescence. J. R. Gallagher and T. L. DeLorme.—p. 847.
Method of Procuring Iliac Bone by Trephine Curettage. W. Scott, R. C. Petersen and S. Grant.—p. 860.
Vitallium-Cup Arthroplasty of Hip Joint. Review of Approximately 100 Cases. A. Gibson.—p. 861.
Posterior Dislocation of Hip with Fracture of Head of Femur. E. J. Gordon and J. A. Freiberg.—p. 869.
Surgical Approach to Vertebral Body. A. A. Michele and F. J. Krueger.—p. 873.

Contact-Compression Factor in Osteogenesis in Fractures.—Eggers and his associates describe animal experiments to determine the influence of a compression force in osseous repair. Each specimen of animal skull presented a field of study in which there was an area of static flap control; a movable flap, to the margin of which the contact-compression factor could be applied; the opposite, noncompressed control flap margin, and an undisturbed skull margin. The experimental technic furnished material which was placed under mechanical stress, applied on a margin of choice. One free margin of the bone flap was compressed anteriorly, but, proceding posteriorly, the degree of compression decreased, and finally there was no contact at all. Thus, material with contact and compression, with contact and excessive pressure and with compression and no contact could be observed. Since it was not possible experimentally to insure contact without some compression, and since it was shown that compression could be produced without contact, the authors selected the terms "contact-compression factor." This factor is, therefore, the combination of contact and the force to promote contact, exerted on bone structures for which osseous union or osteogenesis is desired. The contact-compression factor consists of two parts: (1) contact of surfaces under compression and (2) the compression force, which may be internal or external. The internal force is created by the muscles. The external contact-compression force is due to nonphysiologic forces, such as gravity, weight bearing and surgical methods. The authors produced union and purposeful osteogenesis in surgical fractures by applying the contact-compression factor alone. Microscopic sections are the factual evidence of this accomplishment. Excessive pressure causes necrosis of the compressed bone, and lack of pressure fails to stimulate osteogenesis. The most advantageous compression force on the fracture surfaces probably is exerted by the physiologic forces of the musculature of the parts involved.

Sensory Denervation of Hip.—According to Obletz and his co-workers pain is the major disabling factor in chronic arthritis of the hip, regardless of the cause. Partial denervation of the hip was performed for the relief of pain in various types of chronic arthritis of the hip. The operation consists of an intrapelvic obturator neurotomy and section of the nerve to the quadratus femoris. It is relatively easy to perform and produces no constitutional reaction, so that it is applicable to a large group of patients. Of 42 patients with painful arthritis of the hip who were thus treated, satisfactory relief from pain was obtained in 28. The longest postoperative observation period was twenty months. When obturator neurotomy alone was used for the relief of pain, it was found that the intrapelvic approach was more effective than the extrapelvic operation. Eleven of the 14 patients with poor results in this series were treated by extrapelvic obturator-nerve section. Lack of consistently satisfactory results may be attributed to anatomic variations in the sensory nerve supply to the hip.

Journal of Experimental Medicine, New York

90:373-510 (Nov.) 1949. **Partial Index**

Formation of Bacterial Toxin (Streptolysin S) by Resting Cells. A. W. Bernheimer.—p. 373.
Resistant Variant of Mumps Virus: Multiplication of Variant in Presence of Inhibitory Quantities of Friedländer Bacillus Polysaccharide. H. S. Ginsberg and F. L. Horsfall Jr.—p. 393.
Stabilization of Serum Lipid Emulsions by Serum Phospholipids. E. H. Ahrens Jr. and H. G. Kunkel.—p. 409.
Protein Metabolism and Exchange Influenced by Constriction of Vena Cava: II. Effects of Parenterally Administered Plasma, Amino Acid Mixture, and Ascitic Fluid, and of Orally Administered Ascitic Fluid in Experimental Ascitic Dog. F. W. McKee, R. E. Hyatt, W. G. Wilt Jr. and others.—p. 447.
Bile Salt Metabolism as Influenced by Pure Amino Acids and Casein Digests. W. B. Hawkins, P. C. Hanson, R. W. Coon and R. Terry. —p. 461.
Labile Component of Normal Serum Which Combines with Various Viruses. Neutralization of Infectivity and Inhibition of Hemagglutination by Component. H. S. Ginsberg and F. L. Horsfall Jr. —p. 475.
Lymphatic Contractility: Possible Intrinsic Mechanism of Lymphatic Vessels for Transport of Lymph. R. O. Smith.—p. 497.

Journal of Gerontology, Springfield, Ill.

4:273-360 (Oct.) 1949

Quantitative Measurements of Elastic Properties of Skin and Subcutaneous Tissue in Young and Old Individuals. E. Kirk and S. A. Kvorning.—p. 273.
*Working Life Span of American Workers. E. Clague.—p. 285.
Trends of Employment in Relation to Problems of the Aging. W. H. Stead.—p. 290.
Old Age—An American Problem. R. J. Havighurst.—p. 298.
Medical Care of the Aged. E. M. Bluestone.—p. 305.
Recreation for the Aged. O. Schulze.—p. 310.
European Gerontologic Activities. V. Korenchevsky.—p. 314.

Working Life Span.—Clague shows that, while life expectancy has been steadily increasing in recent decades, there have been no corresponding gains in the working life span. Modern industry and related occupational trends have tended to limit employment opportunities of older workers and to lengthen the period of dependency in old age. If prewar trends continue, a 20 year male worker, in 1975, may expect to spend an average of almost ten years outside the labor force, as compared with five and a half years in 1940 and less than three years in 1900. A program for extension of working life is needed as an alternative to a steady increase in the period of old age dependency and in the corresponding economic burden. This will require concerted community action, in conjunction with employer and labor groups, to secure a much more flexible employment policy geared to the capacities of individual workers.

Journal of Nutrition, Philadelphia

39:1-138 (Sept.) 1949. **Partial Index**

Ascorbic Acid Metabolism of Older Adolescents. C. A. Storvick, B. L. Davey, R. M. Nitchals and others.—p. 1.
Nitrogen Excretion of Women Related to Distribution of Animal Protein in Daily Meals. R. M. Leverton and M. R. Gram.—p. 57.
Iron Requirement of Six Adolescent Girls. D. Schlaphoff and F. A. Johnston.—p. 67.
Growth-Promoting Effect on Rat of Summer Butter and Other Fats. S. Lassen and E. K. Bacon.—p. 83.
Intestinal Synthesis of Niacin and Metabolic Interrelationship of Tryptophan and Niacin in the Rabbit. O. Olcese, P. B. Pearson and P. Sparks.—p. 93.
Urinary Pantothenate, Blood Glucose, and Inorganic Serum Phosphate in Patients with Metabolic Disorders Treated with Doses of Pantothenate. H. Gershberg, S. H. Rubin and E. P. Ralli.—p. 107.

Journal of Pediatrics, St. Louis

35:529-670 (Nov.) 1949

Review of 396 Cases of Acute Diarrhea in Which Early Oral Feedings Were Employed in Treatment. J. E. Mitchell, W. D. Donald and M. Birdsong.—p. 529.
*Tridione Therapy in Epilepsy: Review of Results in 156 Patients with Petit Mal Epilepsy with Special Reference to Side Reactions. H. S. Mustard and S. Livingston.—p. 540.
Aureomycin in Treatment of Acute Bronchiolitis of Infants. B. F. Thompson Jr. and S. Spector.—p. 546.
Syndrome of Cerebral Concussion in Children. M. T. Schnitker.—p. 557.
*Central Nervous System Involvement in Parotitis. M. J. Fox and B. F. Grotts.—p. 561.
Prognosis of Facial Nerve Paralysis in Poliomyelitis. H. Rascoff.—p. 567.
Parasympathicomimetic Drugs in Treatment of Hirschsprung's Disease. M. J. Carson.—p. 570.
*Measles in Nephrotic Syndrome. A. H. Rosenblum, H. B. Lander and R. M. Fisher.—p. 574.
Congenital Cystic Disease of Lung. D. E. Cassels, J. M. Fritz and W. E. Adams.—p. 585.
Coccidioidin Patch Test. R. Cohen and M. A. Gifford.—p. 601.
Criteria of Operability in Tricuspid Stenosis. H. Swan, G. J. Maresh and G. R. Fisher.—p. 604.
Recurrent Meningitis. N. H. Schwartz and F. B. Champlin.—p. 611.

Trimethadione (Tridione®) Therapy in Epilepsy.—Mustard and Livingston treated 156 patients with petit mal epileptic seizures, 6 less than 2 years of age, 94 between the ages of 2 and 14 years and 56 over 14, with trimethadione (tridione®, or 3,5,5-trimethyloxazolidine-2,4-dione). One hundred and four patients (67 per cent) showed definite improvement. Fifty-two either failed to respond favorably or manifested serious toxic effects requiring withdrawal of the drug. Untoward reactions were observed in 62 patients (39.5 per cent). It was necessary to discontinue the drug in 38 of these patients. Eleven of the 66 patients with epileptic seizures of pure petit mal type had their first grand mal seizures soon after the start of trimethadione therapy. In 13 of the 90 patients with seizures of mixed, grand and petit mal type, the grand mal seizures became more frequent and severe soon after the start of treatment. Trimethadione is probably the most effective drug in the treatment of petit mal seizures. The multiplicity of its toxic effects and its apparent tendency to precipitate and also to increase the frequency of grand mal seizures are considerations of which the physician should be aware before prescribing the drug. In addition to trimethadione the patient should be given such anticonvulsants as phenobarbital or diphenylhydantoin sodium. Toxic effects, particularly the development of leukopenia, even one year after the initiation of treatment with trimethadione, must be watched for.

Central Nervous System and Parotitis.—Fox and Grotts report 22 cases of mumps encephalomeningitis in 17 male and 5 female patients between the ages of 10 months and 27 years, who were admitted to South View Isolation Hospital in Milwaukee between January 1940 and February 1949. Symptoms appeared on an average of 4.8 days after the onset of glandular swelling. Fever, headache, vomiting and lethargy or coma were the most common symptoms, while nuchal rigidity, swollen salivary glands and a positive Kernig test were the most important signs. Mumps is a disease characterized by a generalized viremia, in which the virus has a predilection for the salivary glands and meninges. The blood count and sedimentation rate did not appear to be significantly altered. The cerebrospinal fluid cell count averaged 548, 93 per cent of which were lymphocytes. The spinal fluid sugar and protein determinations were normal in most cases, while chlorides tended to be reduced or low normal. Recovery was rapid and complete without any residuals or deaths. The average hospitalization was approximately seven days. All gradations of meningeal involvement may occur, including asymptomatic spinal fluid pleocytosis, symptoms and signs of a typical meningitis and the more unusual and severe encephalitic form of the disease, which resembles choriomeningitis. There appeared to be no correlation between the severity of the signs and symptoms and the cerebrospinal fluid cell count, pressure or chemical composition.

Measles in Nephrotic Syndrome.—Rosenblum, Lander and Fisher report 7 children, 5 boys and 2 girls between the ages of 2 and 7 years, with the nephrotic syndrome of edema, hypercholesterolemia, hypoproteinemia and albuminuria, complicated by measles. Though remissions in the nephrotic syndrome are known to occur spontaneously and after many infections, they were noted most regularly during or following measles. Three of the authors' patients showed decided and lasting improvement, 3 transient improvement and 1 no response. The nephrotic patient who contracts measles may be critically sick. Because of this and because the degree of remission may not be comparable to the severity of illness during measles, it is questionable whether it is wise to expose these patients to measles to obtain relief from the nephrotic syndrome. Preliminary data on the protein chemistry of the 7 patients seem to indicate a trend toward higher total protein levels after the measles. This increase seems to be due to elevations in both the albumin and globulin fractions, although there was considerable variation in the different patients and the rise was not always sustained. Since the formation of antibodies seems to be linked with various protein fractions of the blood, and most usually with the gamma globulin, this fraction may be intimately related to the clinical improvement shown by these patients.

Journal of Urology, Baltimore

62:639-790 (Nov.) 1949. **Partial Index**

Adrenal Cortical Tumor: Case Reports. J. H. Kiefer and I. P. Bronstein.—p. 639.
Renal Carbuncle (Staphylococcal Abscess of Kidney). N. M. Welch and G. C. Prather.—p. 646.
Unilateral Congenital Cystic Kidney in Infant Complicated by Hydronephrosis. L. D. O'Donnell and J. C. Presti.—p. 651.
Transthoracic Nephrectomy for Metastatic Osteogenic Sarcoma of Kidney. D. F. Marshall and E. H. Drake.—p. 655.
Postoperative Stricture and Periostitis Pubis Following Retropubic Prostatectomy. S. F. Wilheim and S. Z. Freed.—p. 660.
Distribution of Blood Vessels of Prostate Gland and Urinary Bladder: Application to Retropubic Prostatectomy. F. A. Beneventi and G. J. Noback.—p. 663.
Interstitial Cell Tumors of Testis: Review of Literature and Report of Case; Discussion of Gynecomastia and Testosterone; Incidence in Animals and Experimental Production of Interstitial Cell Tumors. M. M. Melicow, J. N. Robinson, W. Ivers and L. K. Rainsford.—p. 672.
Atypical Cytology in Testes Biopsies. E. T. Engle.—p. 694.
Torsion of Spermatic Cord. S. Peck.—p. 701.
Surgical Management of Vagina in Male Construction in Hermaphrodites. A. B. Cecil.—p. 709.
Secondary Testicular Tumor Resembling Krukenberg Tumor, Case Report. M. Z. London and S. N. Grossman.—p. 713.
Treatment of Urinary Bladder Diverticula by Marsupialization. J. J. Crane.—p. 719.
Occult Prostatic Carcinoma Diagnosed upon Transurethral Resection. F. Hinman Jr. and F. Hinman.—p. 723.
Endoscopic Identification of Tissue During Transurethral Prostatic Resection. R. W. Barnes and I. E. Martin.—p. 730.
Clinical Comparison of Use of Glucose and Urea in Irrigating Solutions for Transurethral Prostatic Resections. C. E. Ebert.—p. 736.
Solitary Hydrocalyx Secondary to Dumbbell Calculus. J. W. Dorsey.—p. 742.
Renal Sarcoma: Report of Case with Spontaneous Rupture of Kidney. T. O. Powell and J. E. Clark.—p. 751.
Experimental Studies and Clinical Aspects of Renal Circulation. J. A. Arcadi and F. Farman.—p. 756.
Renal Hematuria and Hypoprothrombinemia. C. B. Moore.—p. 762.
*Treatment of Bacillary Urinary Infections with Chloromycetin. G. E. Chittenden, E. A. Sharp, E. C. Vonder Heide and others.—p. 771.

Chloramphenicol (Chloromycetin®) in Urinary Infections.—Chittenden and his associates state that the bacteriologic spectrum of antibiotic activity of chloramphenicol reveals that chloramphenicol is highly effective in the bacillary group of organisms commonly found in both acute and chronic urinary tract infections. Chloramphenicol has the advantage that it may be administered orally and that it is devoid of gastrointestinal, neurotoxic, cutaneous or allergic reactions. The authors review observations on 50 cases, which indicate that there is a much higher percentage of multiple infections than has heretofore been considered. Likewise the coccic groups of organisms are apparently more important than heretofore realized. There is also a peculiar variability of organism strains for which no adequate reason can yet be ascribed. Adjunct therapy with penicillin and the sulfonamide drugs is essential when urinary cultures show coccic organisms in addition to the bacillary forms. The removal of calculi, obstructions, carcinoma and focal sources are necessary for the ultimate and complete control of urinary infections.

Medical Annals of District of Columbia, Washington

18:505-560 (Oct.) 1949

Atomic Bombs Over Washington. L. H. Snyder.—p. 505.
Injuries of Knee Joint. A. F. Voshell.—p. 512.
Tendon Injuries. W. J. Tobin.—p. 516.
Carcinoma in Young Adults. W. H. Graham.—p. 520.
Surgery of Colon: Preoperative and Postoperative Care. E. C. Wilson Jr. and C. S. White Jr.—p. 528.

Nebraska State Medical Journal, Lincoln

34:341-372 (Oct.) 1949

Cushing's Syndrome—Possible Clue to Certain Diseases Associated with Aging. T. Findley.—p. 344.
Toxemias of Pregnancy. G. V. Le Roy.—p. 346.
Socio-Medical Trends in the United States. J. R. McVay.—p. 348.
Trends in Legislation. J. S. Lawrence.—p. 351.
Spinal Anesthesia in Obstetrics. D. H. Thompson.—p. 353.

SYMPOSIUM ON ADOLESCENCE

Physiology of Adolescence. G. O'Neil.—p. 356.
Endocrine Problems of Adolescent. J. F. Gardiner.—p. 357.
Menstrual Variations in Adolescent. L. S. McGoogan.—p. 362.
Emotional Problems of Adolescence. H. M. Jahr.—p. 364.

34:373-404 (Nov.) 1949

Carcinoma of Stomach. C. E. Dunlap.—p. 376.
Sympathectomy and Ischemia Extremity. T. Findley.—p. 379.
Psychiatric Problems in Nabraska's Older People. G. L. Sandritter.—p. 384.
Melanoma. R. A. Hillyer.—p. 386.

New England Journal of Medicine, Boston

241:631-678 (Oct. 27) 1949

Variations in First Apical Sound Simulating So-Called "Presystolic Murmur of Mitral Stenosis:" Phonocardiographic Study. M. M. Alimurung, M. B. Rappaport and H. B. Sprague.—p. 631.
Unsuspected Trauma to Heart During Intrathoracic Surgery. A. L. Ruprecht and A. Adelman.—p. 637.
Acute Gangrenous Cholecystitis. W. J. Clifford.—p. 640.
Kaposi's Varicelliform Eruption: Report of Case. S. S. Freedman and J. T. Barrett.—p. 644.
Mechanical and Thermal Injury from Atomic Bomb. H. E. Pearse and J. T. Payne.—p. 647.
Bronchial Adenoma.—p. 666.
Pulmonary Emboli, Multiple, Recent and Old, with Recanalization.—p. 669.

241:679-724 (Nov. 3) 1949

Pulmonary Embolism: Statistical Study of Post-Mortem Material at Massachusetts General Hospital. B. B. Roe and J. C. Goldthwait.—p. 679.
Plastic Operation on Fallopian Tube. F. M. Ingersoll.—p. 686.
Streptomycin in Treatment of Subacute Bacterial Endocarditis: Review of Literature and Report of Case Caused by Bacteroides. R. Wallach and N. Pomerantz.—p. 690.
*Evaluation of Tolserol in Treatment of Children with Cerebral Palsy. E. Denhoff, R. H. Holden and C. M. Silver.—p. 695.
Oral Administration of Aureomycin in Treatment of Urinary Infections. A. M. Rutenburg and F. B. Schweinburg.—p. 698.
Hemorrhagic Diseases. W. B. Frommeyer and R. D. Epstein.—p. 700.
Adenocarcinoma of Pancreas, with Extension to Stomach and Metastases to Pulmonary Lymphatics.—p. 713.
Tuberculous Salpingitis, Endometritis and Peritonitis.—p. 716.

Mephenesin (Tolserol®) in Cerebral Palsy.—Denhoff and his associates administered mephenesin (tolserol®) dissolved in aqueous propylene glycol and syrup of cherry so that 30 cc. of the solution contained 1 Gm. of the drug. The average dose was 33 mg. per pound of body weight per twenty-four hours. The tolserol mixture was administered by mouth to each child six times a day. The condition of 14 of the 16 patients were diagnosed as spastic, 1 as athetoid and 1 as ataxic. In the classification of neuromuscular dysfunction 2 were considered severe, 11 moderate and 3 mild. The patients were divided into two groups. Those in group 1 received the drug for three weeks, followed by a placebo mixture for another six weeks, and then the drug was readministered for another three week period. The procedure was reversed in group 2. No definite over-all improvement was noted. Improvement was primarily in the neurologic category: 9 of the children showed diminution of exaggerated reflexes; the neurologic condition was worse in 6 and there was no change in 1. The orthopedic status showed slight improvement in 5 patients, remained unchanged in 2 and became worse in 9. Locomotion was improved somewhat in 6 cases. Behavior changes were not appreciable. The drug did not produce toxic effects.

North Carolina Medical Journal, Winston-Salem

10:529-576 (Oct.) 1949

Treatment of Myoma Uteri. R. A. Kimbrough.—p. 529.
North Carolina Academy of General Practice: President's Address. J. R. Bender.—p. 532.
Application of Psychosomatic Techniques to General Practice of Medicine. M. H. Greenhill.—p. 535.
Carcinoma of Stomach. C. E. Gardner Jr.—p. 541.
Thiocyanate Intoxication. E. H. Yount Jr. and E. A. MacMillan.—p. 545.
Problem of Infantile Cerebral Palsy. F. C. McMains.—p. 548.
Diagnosis and Management of Mild and Severe Pre-Eclampsia. L. De Camp.—p. 553.
*Culdoscope in Private Practice. R. B. Dunn and D. C. Schweizer.—p. 556.
Role of Low-Dosage Irradiation in Selected Cases of Menstrual Disorders. G. S. Edgerton.—p. 559.
Traumatic Para-Esophageal Eventration with Report of Case. J. W. Tankersley, A. J. Tannenbaum and S. S. Rogers.—p. 562.

Culdoscopy in Private Practice.—Dunn and Schweizer present their experiences with the culdoscope in 28 cases. They believe the culdoscope is a useful instrument for the obstetrician and the gynecologist. The technical procedure is not difficult, and many patients may be saved abdominal operations by the use of this instrument. It has proved safe. While it has helped to solve many difficult diagnostic problems related to the female pelvis, the authors feel that its greatest usefulness may be in cases of infertility.

Radiology, Syracuse, N. Y.

53:469-624 (Oct.) 1949

Diagnosis of Congenital Heart Disease by Ordinary Methods. M. J. Shapiro.—p. 469.
Conventional Roentgenography in Diagnosis of Cardiovascular Anomalies. D. R. Peck and H. M. Wilson.—p. 479.
Conventional Roentgen Examination in Operable Congenital Heart Disease. H. M. Stauffer.—p. 488.
Clinical Applications of Electrokymography: Findings in Myocardial Infarction and Heart Block. M. L. Sussman, S. Dack and D. H. Paley.—p. 500.
Angiocardiographic Interpretation. C. T. Dotter and I. Steinberg.—p. 513.
Experimental Chemotherapy of Neoplastic Diseases. M. B. Shimkin and H. H. Bierman.—p. 518.
*Action of Steroid Hormones in Mammary Cancer. W. Van Winkle Jr.—p. 530.
Nephrography: Experimental and Clinical Observations. R. S. Leighton.—p. 540.
Roentgen Examination of Hip in Legg-Perthes' Disease. E. H. Bettman and R. S. Siffert.—p. 548.
Sodium Tetraiodophthalicfluorescein for Intravenous Cholecystography. M. J. Smith and G. E. Moore.—p. 552.
Cholecystocolic Fistula. R. H. Marshak and W. Henkin.—p. 555.
*Roentgen Findings in Acute Friedländer's Pneumonia. B. Felson, L. S. Rosenberg and M. Hamburger Jr.—p. 559.
Diaphragmatic Herniation of Kidney: Case Report. R. G. Williams and A. J. Tillinghast.—p. 566.
Survey of Scattered Radiation from Fluoroscopic Units in Fifteen Institutions. R. F. Cowing and C. K. Spalding.—p. 569.

Action of Steroid Hormones in Mammary Cancer.—According to Van Winkle the Therapeutic Trials Committee of the Council on Pharmacy and Chemistry of the American Medical Association has instituted a critical clinical study of the effects of hormone therapy in breast cancer. Participating investigators report their cases to the Committee. This paper reports on 77 patients with cancer of the breast with bony metastases who have received up to one year's treatment. A favorable response to testosterone therapy was noted in 45 per cent although only 13 per cent have shown objective improvement. Testosterone therapy in 17 cases of mammary cancer with only soft-tissue lesions showed a similar incidence of objective improvement, but the degree of subjective response was significantly lower than in cases with bony metastases. Of 21 patients with cancer of the breast receiving estrogen therapy, 5 showed objective improvement. These results are preliminary and will probably be altered as the study progresses. It is not possible at this time to define the place of endocrine therapy in mammary cancer, except to state that it may be tried when all other forms of therapy have been given adequate trial and have failed. Neither androgens nor estrogens should be used in lieu of surgical measures or irradiation.

Roentgenologic Aspects of Acute Friedländer's Pneumonia.—Felson and his associates report 16 cases of acute Friedländer's pneumonia. Fourteen of the patients died, and 13 autopsies were performed. One or more chest roentgeno-

grams were available for study in each case. For purposes of comparison, parallel studies were made out on roentgenograms from 58 patients with acute pneumonia due to other causes, of whom 25 were known to have pneumococcic pneumonia with bacteremia. The latter group of 25 was selected because the severity of the disease approximated that of Friedländer's pneumonia, in which the diagnosis is established by the isolation of the causative organism from the sputum, blood stream, pleural fluid, aspirated pulmonary fluid, or secretions removed bronchoscopically. The size of the affected lobe, the appearance of the margins of the pneumonic infiltrate, the occurrence of abscess formation, the presence of bronchopneumonia, and the radiopacity of the pneumonic shadow were recorded and comparison was made among the three groups of cases. Bulging of a fissure, sharp advancing borders of the infiltrate and abscess formation were found to occur in acute Friedländer's pneumonia with considerably greater frequency than in other types of pneumonia. A purely bronchopneumonic form of Friedländer's pneumonia was not encountered in this series. The pneumonic infiltrate in the Friedländer group was relatively radiopaque, but shadows of similar density were commonly found in other types of pneumonia. Although the roentgenologic observations in Friedländer's pneumonia are not pathognomonic, in many instances it is possible to suggest the correct diagnosis from the roentgenogram.

Review of Gastroenterology, New York

16:743-808 (Oct.) 1949

Unusual Complication Following Radical Pancreaticoduodenectomy. A. J. A. Campbell and S. Mikal.—p. 757.
Bictoxic Intestinal Conditions of Putrefactive Type. A. Bassler.—p. 764.
*Lipotropic Agents in Treatment of Liver Dysfunction of Diabetes Mellitus. J. Pomeranze and V. Levine.—p. 771.
Psychosomatic Aspects of Pruritus Ani. A. J. Cantor.—p. 778.
Further Studies on Liver Function Tests in the Aged. H. Rafsky and B. Newman.—p. 783.
Idioblaptic Diseases of Alimentary Tract. A. F. Coca.—p. 786.

Lipotropic Agents in Diabetes Mellitus.—According to Pomeranze and Levine it is widely held that many persons developing hyperglycemia after the third decade really have low grade liver damage rather than insulin deficiency, as implied in a diagnosis of diabetes. They report studies on 6 diabetic patients who had evidence of hepatic dysfunction. Studies on the blood included determinations of cholesterol and cholesterol esters, total protein and albumin and globulin, quantitative van den Bergh, thymol turbidity and alkaline phosphatase. These were repeated frequently during the treatment period. Treatment was started after the initial laboratory tests and consisted of a diet high in protein and low in fat. Insulin intake was continued when previously given and regulated according to urinalysis. Two therapeutic formula vitamin capsules were given daily. Lipotropic therapy consisted of 18 methischol® capsules daily, divided into three doses, which provided 3.6 Gm. of choline dihydrogen citrate (1.5 Gm. of choline), 2 Gm. of methionine, 1 Gm. of inositol and the extract from 72 Gm. of liver. In some of the cases the daily dosage was halved after a period. There was a favorable chemical response to therapy, the levels in all patients reverting to normal. These cases suggest that liver dysfunction is common in diabetes.

Rocky Mountain Medical Journal, Denver

46:889-992 (Nov.) 1949

Speculum Medici. R. Fitz.—p. 908.
Otology in General Practice. H. I. Laff.—p. 914.
SYMPOSIUM ON PUBLIC HEALTH PROGRESS IN COLORADO
I. Present Administrative Organization and New Programs. R. L. Cleere.—p. 918.
II. Phases of Program of Public Health Dentistry. R. A. Downs.—p. 921.
III. Colorado Veterinary Public Health Program. M. D. Baum.—p. 923.
IV. Sanitation Program in Colorado. J. A. King.—p. 924.
V. Local Health Departments and Physician. R. H. Loder.—p. 926.
Trichomoniasis in the Male. R. L. Young.—p. 928.
Isotopes and New Alchemy. T. P. Sears and K. D. A. Allen.—p. 931.
Medicolegal Aspects of Radiation Injury. S. Warren.—p. 936.
Biologic Aspects of Atomic Energy. S. Warren.—p. 937.

South Carolina Medical Assn. Journal, Florence

45:303-334 (Oct.) 1949

Chronic Diseases of Thyroid. W. C. Cantey and E. C. Kinder.—p. 303.
Report of American Academy of Pediatrics Study of Child Health Services in South Carolina. J. I. Waring.—p. 308.

45:335-358 (Nov.) 1949

Obstetrical Lessons from Studies of Maternal Mortality. J. D. Guess.—p 335.
Convulsions in Childhood. J. A. Toomey.—p. 338.
Special School Therapy for Problem Adolescent. L. R. Angus.—p. 339.
New Antihistaminic—Chlor-Trimeton Maleate. J. R. Allison and A. M. Robinson.—p. 344.

Surgery, Gynecology and Obstetrics, Chicago

89:529-656 (Nov.) 1949

Experimental Ascites: Effects of Sodium Chloride and Protein Intake on Protein Metabolism of Dogs with Constricted Inferior Vena Cava. F. W. McKee, J. A. Schilling, G. H. Tishkoff and R. E. Hyatt.—p. 529.
*Postphlebitic Leg: Results with Femoral Vein Interruption. S. T. Glasser.—p. 541.
Modern Surgeries of Prostate. C. L. Deming.—p. 547.
Endometrium in Old Age. H. Speert.—p. 551.
Treatment of Slipping of Upper Femoral Epiphysis: Study of Results of 42 Cases. C. H. Heyman.—p. 559.
Fluorescein as Adjunct in Treatment of Radionecrotic Ulcers. B. S. Freeman.—p. 566.
Use of Urecholine in Prevention of Postoperative Distention. C. E. Stafford, A. I. Kugel and A. Dederer.—p. 570.
Comparison of Pain Produced Experimentally in Lower Esophagus, Common Bile Duct and Upper Small Intestine with Pain Experienced by Patients with Diseases of Biliary Tract and Pancreas. W. P. Chapman, R. Herrera and C. M. Jones.—p. 573.
*Local and Systemic Effects of Chronic Ulcerations. L. T. Byars and G. S. Letterman.—p. 583.
Regional Lymph Node Dissection in Cancer of Extremities. J. H. Frieden.—p. 591.
Transthoracic Nephrectomy (Right) for Tuberculosis of Kidney. V. J. O'Conor and J. R. Head.—p. 599.
Use of Free Peritoneal Grafts in Intestinal Anastomoses. S. T. Chester, H. G. Bell and H. J. McCorkle.—p. 605.
Effect of Intramedullary Nailing on Healing of Fractures: Experimental Study. W. T. Fitts Jr., B. Roberts, S. I. Spoont and V. W. Ritter.—p. 609.
Histochemical Studies on Glycogen in Carcinoma in Situ of Cervix Uterii. J. F. A. McManus and L. Findley.—p. 616.
Simultaneous Prostatectomy and Inguinal Herniorrhaphy. D. F. McDonald and C. Huggins.—p. 621.
Removal of Auricular Appendage in Dog. W. J. Burdette.—p. 623.
Aspects of Development of Intrathoracic Surgery. C. Crafoord.—p. 629.
Simplified Treatment of Ingrown Toenail. R. W. Newman.—p. 638.
Production and Prevention of Thrombosis and Embolism. E. C. Mason and S. P. Harrison.—p. 640.

Interruption of Femoral Vein After Phlebitis.—Glasser reports on 71 patients, in 20 of whom the operation for interruption of the femoral vein after phlebitis was bilateral. The origin of the primary thrombophlebitis was indefinite in so many cases that a comparative percentage of incidence relative to either postpartum, postoperative or postmedical source could not be ascertained. The postphlebitic state had lasted for three to thirty years. The author stresses the importance of individualization in the treatment, pointing out that the varied pathologic aspects manifested by sequelae in different stages require varied therapeutic procedures or a combination of treatments. Various surgical procedures are discussed. Especial emphasis is placed on the importance of ligation of the femoral vein immediately distal to the profunda branch, as the author employed it in ninety-one ligations on 71 patients. There were no surgical deaths. Two infected wounds cleared within one week. The only annoying symptom was pain along the distal course of the femoral vessels, particularly over the inner aspect of the knee. The pain lasted four to ten days. Moderate postoperative edema was present in 12 cases. The swelling usually subsided in one week, but in 1 instance six months elapsed before the edema subsided. Follow-up was possible in only 40 of these cases. The results were satisfactory. The author considers femoral vein ligation the one therapeutic measure which is essential in the treatment of the postphlebitic state.

Effects of Chronic Ulcerations.—Byars and Letterman state that loss of a partial thickness of skin should be followed by quick healing, since epithelial regeneration takes place from the deeper elements. When a full thickness of skin has been lost, healing progresses by two processes. There is an epithelial ingrowth from the remaining intact skin at the margins of the wound. Simultaneously with epithelial growth, granulation

tissue is forming from the base of the wound, and this tissue is converted into scar which contracts. The base of the wound is pulled together and is reduced in size so that the area which must be epithelized is thereby diminished. Although this process may be life saving, it is also deforming; it causes the contracture, the ectropion of the eyelid or the distortion of an extremity. The more dense the scar tissue and the greater its age, the less vascular it becomes. The chronic ulcer is soon surrounded by a cortex of dense, avascular scar which prevents further healing. The only adequate approach is excision of the entire ulcer. The scar must be removed down to tissue of adequate vascularity. This newly created wound should be covered with skin, preferably at the time of excision, in order to produce immediate healing of the area with tissue of good quality. The systemic effects of chronic ulceration are those of general weakness with weight loss, infection, hypoproteinemia, anemia, pain, fever, inability to take and metabolize adequate amounts of food, and loss of morale through pain and disability. An understanding of the many problems involved leads one to believe that the search for a magic drug which may be applied topically to eliminate scarring and speed healing will be of no avail. A permanently healed wound is the only satisfactory solution of the problem of chronic ulcer; this may be obtained at the earliest possible moment by the use of split-thickness skin grafts.

Surgery, St. Louis

26:567-726 (Oct.) 1949

*Treatment of Advanced Mammary Cancer with Estrogens. M. Cutler, M. Schlemenson, J. J. Kearney and E. Caceres.—p. 567.
Mammaplastic Substitute for Amputation in Hypertrophies. J. W. Maliniac.—p. 573.
Implications of Local Excision or Simple Mastectomy Prior to Radical Mastectomy for Carcinoma of Breast. C. E. Lockhart and L. V. Ackerman.—p. 577.
*Cancer of Rectum. H. E. Bacon.—p. 584.
Principles Affecting Successful Esophageal Anastomosis: Report of 23 Operations, Without Operative Mortality. G. McNeer.—p. 590.
Traumatic Iliac Hernia with Extensive Soft Tissue Loss. M. L. Lewin and E. T. Bradley.—p. 601.
Henry Approach to Femoral Hernia: Report of 2 Cases. J. E. Musgrove and F. J. McCready.—p. 608.
Resection of Segments of Auricular Wall: Experimental Study. A. Brunschwig and G. F. Robbins.—p. 612.
Delayed Primary Closure of Contaminated Wounds: Report Based on 46 Cases. J. H. Morris and G. H. Martin.—p. 616.
Streptomycin Therapy in Established Wound Infections. E. J. Pulaski and J. F. Connell Jr.—p. 622.
Nephrotoxicity of Bacitracin in Man. A. J. Michie, H. A. Zintel, R. A. Ma and Others.—p. 626.
Local Reaction to Oxidized Cellulose and Gelatin Hemostatic Agents in Experimentally Contaminated Renal Wounds. F. Hinman Jr. and K. O. Babcock.—p. 633.
Spontaneous External Biliary Fistulas. C. L. Henry and T. C. Orr Jr.—p. 641.
Hormone Preparations in Treatment of 282 Mann-Williamson Dogs. D. J. Sandweiss and H. C. Saltzstein.—p. 647.
Osteoplastic Mobilization of Ilium: New Operative Approach to Interior of True Pelvis. H. Bruecke and H. Moser.—p. 653.
Trigger Finger Produced by Excesive Heat. D. Engel.—p. 659.
Radiodermatitis and Necrosis. T. D. Cronin and R. O. Brauer.—p. 665.
Ligament of Treitz as Barrier to Intestinal Intubation: Clinical and Anatomic Study. M. O. Cantor.—p. 673.
Compounds of Zirconium for X-Ray Media. S. W. Hunter, J. Miree and H. Bloch.—p. 682.

Estrogens in Treatment of Advanced Cancer of the Breast.—Cutler and his associates report results in 20 consecutive cases of advanced cancer of the breast treated with estrogens. Palliative effects were obtained in 7 patients, most of whom were over 60 years of age. The effect was evident in both bone and soft tissue metastases. Several estrogenic substances were used, but no difference in response was noted. The optimal doses were not established. Vaginal bleeding occurred in some patients. The duration of palliation has not as yet been determined. The authors gained the impression that certain patients with advanced cancer of the breast experience relief from pain and a sense of well-being during estrogen therapy, even in the absence of objective improvement. There was no evidence that estrogens can cure cancer of the breast.

Cancer of Rectum.—Bacon reviews observations on 800 personally observed patients with cancer of the lower bowel; radical resection was performed in 638 of these. Excision by the abdominoperineal method with the establishment of a permanent abdominal stoma, preferably by the method of Miles, is recommended for all growths involving the anal canal and lowest 3 cm. of the rectum, and no attempt should be made to preserve the sphincter musculature for lesions in this area. Cancerous processes cephalad to this site may be removed by the procedure designated by Miles, although the author's preference is for proctosigmoidectomy, which, for those who master the technic, is suitable for ampullary growths of the rectum, the rectosigmoid and the terminal pelvic colon. An experience of eight years, during which period this method was employed in 401 patients with cancer, provides evidence that the operative mortality rate is low, the period of morbidity diminished and the five year rate of survival parallels, and in some instances, is better than that obtained by the Miles and other procedures. The incidence of local recurrence is greater by less than 2 per cent in comparison with results in the exhaustive investigations of Gilchrist; sexual impotence in the male is decreased, and anal sphincter function is satisfactorily uniform.

Texas State Journal of Medicine, Fort Worth

45:729-794 (Nov.) 1949

Malignant Melanoma of Skin. L. V. Ackerman.—p. 735.
Britain's Gamble in Government Medicine. W. A. Richardson.—p. 744.
Texas State Department of Health, 1907-1911. W. M. Brumby.—p. 748.
Discharges from Vagina: Treatment in Private Practice. G. G. Passmore.—p. 750.
Carcinoma of Uterine Cervix: Clinical Course and Pathologic Basis. J. A. Wall.—p. 754.
Evaluation of Culdoscopy. F. Rutledge.—p. 757.
Conservative Gynecologic Surgery. J. N. Burditt.—p. 759.
Preservation of Ovarian Tissue in Gynecologic Surgery. R. G. Swearingen.—p. 763.

Virginia Medical Monthly, Richmond

76:557-610 (Nov.) 1949

Future of Medicine in Virginia. M. P. Rucker.—p. 559.
Advantages and Limitations of Hormone Therapy in Benign and Malignant Prostatism. L. D. Keyser.—p. 564.
Meningitis in Infancy. W. B. McIlwaine III and H. Farber.—p. 574.
Pre-Operative Study of Malformed Nose. W. L. Gatewood.—p. 579.
Etiological Factors in Pancreatitis. J. B. Floyd Jr.—p. 583.
Optochiasmatic Arachnoiditis: Report of Case. M. B. Raiford.—p. 586.
*Treatment of Bacterial Endocarditis: Review of 12 Cases. R. K. Williams and K. Nelson.—p. 589.
Treatment of Post-Thrombophlebitic Sequelae in Lower Extremities. E. L. Lowenberg.—p. 594.

Treatment of Bacterial Endocarditis.—Williams and Nelson treated 12 patients for bacterial endocarditis at the Medical College of Virginia since 1944. In 5 instances of endocarditis caused by alpha-hemolytic streptococci in patients presumed to have rheumatic heart disease, sterility of the blood was readily obtained with penicillin. In 1 of the 5 patients clinical but not bacteriologic recovery was obtained twice with small doses of penicillin; subsequently, larger and more protracted dosage resulted in sterility of the blood; however, this patient progressively grew worse and died from cardiac failure six months after treatment. In 3 of the 5 patients petechiae and/or embolic phenomena were noted several days to weeks after the blood cultures showed no growth, and in 1 of these the manner of death suggested embolism. In 2 cases there were short periods of inexplicable elevation of temperature after recovery. There were 2 cases of endocarditis due to alpha-hemolytic streptococci in patients with patent ductus arteriosus. Both patients recovered after treatment with penicillin and repair of the congenital defect. In 1 of the 2 cases of endocarditis due to nonhemolytic streptococci recovery was prompt; in the other case there was a gradual downhill course with death from sepsis and cardiac failure. Treatment failed in 3 cases of endocarditis in which the clinical course made this diagnosis certain (2 proved at autopsy) but organisms were not obtained.

Wisconsin Medical Journal, Madison

48:965-1048 (Nov.) 1949

Clinical Evaluation of Serologic Tests for Syphilis. J. M. Lublitz.—p. 988.
Selection of Patients for Sympathectomy. J. A. Evans.—p. 991.
Sporotrichosis: Report of 2 Cases in Unusual Locations. W. B. O'Connor.—p. 997.
Neuroblastoma: Report of Case. J. R. Schroeder.—p. 1000.
Foreign Body in Esophagus Causing Obstruction Simulating Carcinoma: Report of Case. M. W. Nelson and W. Weisel.—p. 1002.
Massive Pulmonary Collapse Following Anesthesia with Curare. R. Foregger, H. Rettig and C. Conroy.—p. 1004.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

61:315-358 (Oct.) 1949

Experimental Assessment of Therapeutic Efficiency of Antifungal Substances. S. R. M. Bushby and S. M. Stewart.—p. 315.
Pityriasis Versicolor with Subsequent Leucodermic Patches. H. G. Adamson.—p. 322.
Pulmonary Fibrosis in Scleroderma. J. E. M. Wigley, V. Edmunds and R. Bradley.—p. 324.

British Journal of Plastic Surgery, Edinburgh

2:145-218 (Oct.) 1949. **Partial Index**

Treatment of Major Injuries of the Hand. E. M. Evans.—p. 150.
Anatomy and Function of Extensor Complex. F. Braithwaite, G. D. Channell, F. T. Moore and J. Whillis.—p. 175.
Suggested Explanation of Non-Healing Traumatic Ulcer. M. Douglas.—p. 188.
Columella. H. Gillies.—p. 192.
Rapid Transfer of Abdominal Tubed Pedicles. W. Hynes.—p. 202.

Glasgow Medical Journal

30:341-384 (Oct.) 1949

Tissue Grafts. G. M. Wyburn.—p. 345.
Observations on Bone Transplants in Anterior Chamber of Eye. J. Hutchison.—p. 357.
*Liver Tumours in Mice Injected with Commercial Food Dyes. A. H. M. Kirby and P. R. Peacock.—p. 364.
Retropubic Prostatectomy: Operation in Men of Seventy-Five or More Years of Age. A. Jacobs.—p. 373.

Liver Tumors in Mice Receiving Food Dyes.—Kirby and Peacock feel that in view of the carcinogenic properties of some azo dyes, it is unwise to assume that synthetic food dyes or flavors are harmless on the basis of short-term toxicity tests. They investigated two commercial dyes at present widely used in Britain for coloring margarine. These dyes are sold under the names of "oil orange E," which is commercial benzene-azo-beta-naphthol, and "oil yellow HA" (formula not published). The molecular structure of benzene-azo-beta-naphthol is related both to the powerful hepatotropic carcinogens orthoamino-azotoluene and para-dimethylaminoazobenzene (butter yellow), and to the vesicotropic carcinogen, beta-naphthylamine. Though the obvious way to test a food dye would be by feeding experiments, there are practical difficulties in administering a prescribed daily dose over a long period to laboratory animals. The characteristic hepatotropic action of certain azo dyes can be demonstrated by their subcutaneous injection into mice. The authors resorted to this method. The occurrence of 7 hepatomas among 24 survivors after fourteen months in the group given injections of "oil orange E" is significant. The single case of hepatoma in one mouse which died on the five hundred and fifteenth day in the group given injections of "oil yellow HA" may be fortuitous; but the occurrence of a spindle cell sarcoma at the site of injection in another mouse in the same group suggests that this substance is a carcinogen, though less potent than benzene-azo-beta-naphthol.

Lancet, London

2:775-822 (Oct. 29) 1949

The Doctor's Creed: Address to Medical Students. G. Fisher.—p. 775.
*Topectomy: Treatment of Mental Illness by Frontal Gyrectomy or Bilateral Subtotal Ablation of Frontal Cortex. J. L. Pool.—p. 776.
Self-Administered Analgesia in Labour with Special Reference to Trichlorethylene. E. H. Seward.—p. 781.
*Synthetic Oestrogens in Mammary Cancer. A. L. Walpole and E. Paterson.—p. 783.
Peripheral Skin Temperature in Normal Pregnancy. C. C. Burt.—p. 787.
*Serum Acid Phosphatase in Diagnosis of Carcinoma of Prostate. C. T. A. Burgess and R. W. Evans.—p. 790.
Acute Polyarteritis Nodosa in Childhood. A. W. Taylor and N. M. Jacoby.—p. 792.
Choice of Test-Meal. J. N. Hunt.—p. 794.

Topectomy.—According to Pool, topectomy can be described as frontal gyrectomy or bilateral subtotal ablation of the frontal cortex. The following reasons induced him to perform topectomies rather than lobotomies: 1. It was hoped that relatively small cortical ablations would prove more specific as regards the site and extent of the lesion and might therefore yield equally good therapeutic results without as much cerebral dysfunction. 2. By variation of the site and extent of cortical excisions information might be obtained regarding the role of various portions of the frontal lobes in mental illness. 3. Studies during these operations would shed light on other functions of the frontal lobe. In 125 topectomies performed by him there was not a single death from the operation. Other advantages are better localization of the lesion and a better estimation of its extent; less risk of serious postoperative personality changes, and a better opportunity for studying the functions of the frontal lobes. Both the site of the cortical ablation and its quantity are important factors in determining the success of the procedure. About 44 per cent of all topectomy patients have maintained significant improvement for periods of one to nearly three years. The disadvantages of topectomy are the relatively high incidence of postoperative convulsions (14 per cent in this series) as compared with 10 to 12 per cent after frontal lobotomy and the fact that the operation takes longer.

Synthetic Estrogens in Mammary Cancer.—Walpole and Paterson direct attention to the wide variation in the response of patients with advanced mammary cancer to treatment with synthetic estrogens. In a small proportion of cases there was a dramatic improvement; in others the effect was not so striking but some arrest of the disease resulted, while in the remainder the disease pursued its course unaffected by the treatment. In all patients in whom improvement occurred it was only temporary. In the 50 postmenopausal women with advanced mammary cancer in whom the authors studied the response to synthetic estrogens, they found that clinical improvement was greatest in the older patients and in those receiving the higher doses of estrogen. Vaginal keratinization was also more pronounced in the older patients but was not correlated with dosage. The mechanism of action of estrogens in mammary cancer is still obscure. Since their therapeutic effects in cancer are limited to tumors associated with the reproductive system (prostate and breast), there is no evidence for regarding them as general inhibitors of tumor growth. Probably many factors contribute to the wide variation in response. The histologic grading may be important. The authors have not explored the importance of the histologic factor but consider factors associated with age important. In many of the treated patients the vaginal and mammary tissues may be inherently insensitive to estrogens. The inhibition may be due to antihormones elaborated by the body or by the malignant cells which counteract their action. Progesterone or androgens in sufficient concentration could have this neutralizing effect.

Serum Acid Phosphatase in Carcinoma of Prostate.—Burgess and Evans investigated the preoperative serum-acid-phosphatase levels in 33 cases of benign prostatic hypertrophy, 4 cases of adenocarcinoma of the prostate and 11 cases clinically diagnosed as cancer of the prostate with or without metastases in bones. Prostatic malignant disease was often associated with a normal serum-acid-phosphatase level, and the test was of little value in the clinical assessment of most cases. A low serum-acid-phosphatase level cannot be accepted as evidence of the benign character of a prostatic tumor.

2:823-868 (Nov. 5) 1949

*Significance of Functional Differentiation in Mammary Tumours. B. D. Pullinger.—p. 823.
*Treatment of Brain Abscess with Special Reference to Conservative Method. L. C. Oliver and W. L. B. Leese.—p. 828.
Continuous Spinal Block in Puerperal Hypertensive Encephalopathy with Anuria. R. Bryce-Smith, E. H. Seward, E. A. Williams and others.—p. 831.
Haemolytic Anaemia Associated with Hodgkin's Disease. R. J. K. Brown and M. J. Meynell.—p. 835.
Heat Cramps. W. S. S. Ladell.—p. 836.
Asphyxia and Shock in the Newborn. A. D. T. Govan.—p. 839.
Fatal Asphyxia from Intratracheal Rupture of Tuberculous Mediastinal Lymph-Gland. H. Angelman and W. M. L. Turner.—p. 842.

Functional Differentiation in Mammary Tumors.—Pullinger gives an account of what may be learned from an experimental study of functional differentiation in the mammary gland and its tumors. Two groups of observations were made. The

first group was based on attempts at assessment of the relationship of dosage and response between estrone and the mammary glands of spayed mice at puberty. Results indicated that lobular-alveolar or acinus formation and secretion depended on a specific stimulus applied in adequate quantity. There was no response in the absence of a specific stimulus. The second set of observations concerned the property of spontaneous mammary carcinomas of mice to differentiate into acini and produce secretion and to retain these characteristics when grafted into male mice or female mice that had had ovariectomy. The conclusion was reached that this response is also most probably due to intracellular production of an estrogen-like substance. In inherited tumors of mice due to the Bittner agent, it is conceivable that the agent, in combination with mammary cells, is producing some such substance. In agent-free tumors, the suggestion is made that a heritable change in chemical productivity has occurred in the mammary cells, resulting in the production by the cell of its own chemical stimulus to division and differentiation. The role played by viruses such as the Bittner agent, the stimulus to cell division and the change in cell chemistry are discussed.

Conservative Treatment of Brain Abscess.—Oliver and Leese believe that there is no single method of treatment of brain abscesses applicable to all cases. Aspiration and penicillin replacement, without excision, reduces the risk to life and function to a minimum and is recommended for the majority of brain abscesses. Eight cases are presented to support these views. Aspiration and penicillin replacement without excision of the abscess produced a cure in 6 cases, and in 2 of these only one needling was necessary. In the other 2 cases excision of the abscess could not be avoided.

Medical Journal of Australia, Sydney

2:409-444 (Sept. 17) 1949. **Partial Index**

Hyperventilation Syndrome. W. A. Dibden.—p. 409.
Toxicity of Drugs Used in Local Anesthesia with Report of Fatal Case. J. F. McCulloch.—p. 416.
Use of Urethane in Leuchaemia. I. Collins.—p. 420.
Otogenic Brain Abscess. V. Bulteau.—p. 423.
Observations on Biopsy Studies in Diseases of Gall-Bladder and Obstructive Jaundice. J. W. Perry.—p. 427.

2:445-480 (Sept. 24) 1949. **Partial Index**

Carbon Dioxide Therapy in Clinical Medicine. V. Wynn.—p. 448.
Case of Cavernous Sinus Thrombosis Complicated by Meningitis. B. Venner.—p. 452.
*Continuous Intragastric Drip in Treatment of Peptic Ulcer. H. W. Garlick.—p. 453.
Radiological Investigation of Weight-Bearing Changes in Human Foot. G. McL. Turnbull.—p. 455.
Post-Operative Management and Complications of Retropubic Prostatectomy. D. B. Duffy.—p. 459.
Early Clinical Diagnosis of Carcinoma of Lung. I. Monk.—p. 461.

Continuous Intragastric Drip in Peptic Ulcer.—Garlick states the belief that the intragastric drip therapy of peptic ulcer, suggested by Wicklestein in 1932, should be used more often. The method neutralizes gastric hydrochloric acid continuously. It requires a milk mixture, Rehfuss tube, bottles, dripper, screw clip, rubber tubing and glass connections. The flow is regulated to maintain a continuous drip throughout the twenty-four hours of the day and provides a total volume of approximately 5 pints (2,366 cc.). Pain which is not relieved by a routine ulcer regimen, in particular that caused by a penetrating ulcer, is one indication for the use of this therapy. In a case of this type the intragastric drip did not cure the penetrating ulcer, but it restored the patient to a state of health which enabled him to withstand a partial gastrectomy. Pyloric stenosis is a second indication. In these cases a liquid diet administered by continuous drip passes through the narrowed pylorus, whereas solid food is vomited. In pyloric stenosis with vomiting there is frequently salt deficiency, which can be corrected by the addition of salt to the milk mixture. The author cites a patient who was thin and dehydrated as a result of pyloric stenosis. He was adequately prepared for operation by the continuous intragastric drip therapy. The milk mixture is a high caloric one enabling the patient to receive 4,000 calories from 5 pints (2,366 cc.) of fluid in twenty-four hours. Feeding by this method is well tolerated for a period of three weeks.

Medizinische Klinik, Munich

44:1301-1332 (Oct. 14) 1949. **Partial Index**

New Concepts on Pathogenesis of Strabismus. H.-F. Piper.—p. 1307
*Modification of Sexual Function Inclusive of Spermiogenesis by Interventions on Lumbrosacral Sympathetic. T. Burckhart and A. Schmitt.—p. 1310.
Treatment of Pneumonias That Are Resistant to Sulfonamide and Penicillin. H. Maske and G. Schimert.—p. 1315.
Gonorrheal Vulvovaginitis in Children: Treatment by Penicillin and Estrogens. W. Kiessling.—p. 1318.
New Technic of Strophanthin Therapy. K. Weidner.—p. 1321.

Modification of Sexual Function by Sympathectomy.—Burckhart and Schmitt report 4 patients who had undergone lumbar sympathectomy for endangiitis obliterans. Although these patients showed some impairment of the sexual function, the authors believe that it was not necessarily the intervention on the sympathetic that was responsible. Impairment of the general condition, great exertion, physiologic involution, acute febrile and chronic weakening disorders, as well as disorders of the nervous system and mental disturbances, might be responsible and should be ruled out before sympathectomy is held entirely responsible for the disturbances in the sexual function and spermatogenesis. The authors advise preoperative and postoperative examinations to determine whether operations on the lumbosacral sympathetic chain are likely to impair the sexual function.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

93:3381-3456 (Oct. 1) 1949. **Partial Index**

Esophageal Hiatus Hernia. J. F. Nuboer.—p. 3384.
Diagnosis of Adrenocortical Disorders. A. Querido.—p. 3391.
*Toxicity of "Cold Wave" Solution. A. P. J. van der Burg.—p. 3400.
*Introduction to Clinical Electroretinography. H. E. Henkes.—p. 3416.

Toxicity of Cold Wave Solutions.—Van der Burg reports a hairdresser, aged 22, who complained that for a year she was troubled with poor appetite, discomfort and dizziness. There was irritation of the eyes and a lame and tired feeling in the arms. The woman had been a hairdresser for three years, and for about a year she had worked practically every day with cold wave solution. The first few months that she had worked with these solutions she had red and swollen hands. This disorder subsided after she began wearing a rubber glove on the hand that came most in contact with the cold wave solution and a finger stall on the most exposed finger of the other hand. Cold wave solutions contain thioglycolic acid. The toxicity of these preparations were reported by the Food and Drug Administration of the United States. Cases were reported by authors from The Netherlands. In view of the extremely wide use of these preparations, the incidence of complications appears to be low. In the reported case hypersensitivity played a part. It is important to use special care to avoid absorption of the cold wave solution.

Electroretinography.—According to Henkes the electroretinogram can be regarded as the electric "answer" of the retina to a light stimulus. Although electroretinography has been known for eighty years, only in the last few years, since the contact lens has been used as the lead or derivation electrode, has the method assumed clinical importance comparable to that which electrocardiography has in cardiology. The essential difference between electroretinography and electrocardiography is that in electroretinography recordable differences in electrical potential are produced by a light stimulus. The electroretinogram is registered by means of a modified Elmquist electrocardiograph. A light flash of 20 or 80 luxes for 0.04 second serves as the stimulus. The electrodes are placed (1) on the cornea (by means of a contact lens filled with isotonic solution of sodium chloride), (2) on the forehead and (3) on the eyelid-holder. The author reproduces and explains electroretinographic records and presents clinical histories of 4 patients in whom electroretinographic records were made. These histories demonstrate that the method may eventually avoid useless operations. The clinical use of electroretinography is in its beginnings, its use thus far being restricted to Stockholm and Rotterdam.

Praxis, Bern

38:903-932 (Oct. 13) 1949

*Danger of Mercury Preparations in Therapy of Ascariasis. G. Fanconi and H. Morf.—p. 903.
Feeding of Infants with Consideration of the Use of Partially Skimmed Milk. M. Neyroud and R. M. Du Pan.—p. 907.
*Epidemic of Enterocolitis of the Newborn in Luzern Hospital in 1945. M. Burkard.—p. 912.
Prognostic Value of Blood Sedimentation in Chronic Osteomyelitis. J. Michail and E. Stéphanidis.—p. 921.

Danger of Mercury Preparations in Therapy of Ascariasis.—Fanconi and Morf say that, although ascarides may occasionally produce eosinophilic pulmonary infiltration, eosinophilic leukemoid, urticaria, ileus, abscess of the liver or peritonitis, they are on the whole harmless parasites. Lesions caused by mercury preparations used in their treatment are more frequent than those caused by the ascarides themselves. In young children allergic reactions to mercury are frequent. Usually the early reaction is an acute exanthematic mercurial disorder, which the authors designate as calomel disease. This disorder occurs not only after the oral administration of mercury but after prolonged administration of mercurial ointments. It begins with fever and general malaise and is followed by an exanthem which is scarlatiniform at first and then becomes morbilliform and urticarial. The condition may be mistaken for scarlet fever or measles. Many cases of infectious erythema are probably caused by calomel. The early reaction may take the form of a generalized dermatitis of an eczematoid type. The late reaction frequently takes the form of Feer's disease, known also as erythredema polyneuritis. If a thorough history is taken in Feer's disease and in the calomel disease, and if skin tests are made with mercury, and the urine is examined for mercury, the connection will become apparent. The authors believe that certain forms of radiculoneuritis, as well as lipoid nephroses, may also result from mercury medication. They warn against the use of mercury preparations in young children. BAL (British anti-lewisite), or 2,3 dimercaptopropanol, has been found effective in Feer's disease by American authors.

Epidemic of Enterocolitis of the Newborn in Luzern.—Burkard reports an epidemic of enterocolitis in the newborn in an obstetric ward in Luzern in 1945. Of 104 children who contracted entercolitis, 25 died. The enteric disorder began shortly after birth with anorexia, vomiting and diarrhea. In severe cases there was rapid loss of weight, dehydration and coma. The disorder appeared almost exclusively in artificially fed infants; only 10 per cent were exclusively breast fed. Necropsy revealed that death was caused either by gastroenteritis or enterocolitis; ulcerations were frequent. Fatty degeneration of the liver was present in all cases, and acute cerebral edema and foci of encephalitis were noted in many. Pneumonia was a frequent complication. Treatment consisted chiefly of dietetic measures. In severe cases sulfonamide drugs and plasma transfusions were given. The epidemic was arrested after proper prophylactic measures were taken. Bacteriologic studies were negative. The assumption that the infection was caused by human milk infected with staphylococci was not proved. Several factors speak for an alimentary toxic disturbance in the presence of artificial feeding with excessive amounts of carbohydrates and with a secondary endogenous infection with organisms of the intestinal flora. A search for a virus was not made, but the author considers a virus infection possible.

Presse Médicale, Paris

57:817-832 (Sept. 17) 1949

*Surgery and Treatment with Synthetic Antithyroid Drugs: Inconveniences and Risks of Medication. H. Welti.—p. 817.
*New Symptomatic Drug for Treatment of Parkinson's Syndrome: 10-(2-Diethylaminopropyl) Phenothiazine Hydrochloride. J. Sigwald.—p. 819.

Surgery and Synthetic Antithyroid Drug Therapy.—Welti reports on 2,631 thyroidectomies performed from 1945, when antithyroid drugs were first introduced in France, to 1949. In 1,489 patients operated on, goiters were associated with hyperthyroidism; 1,142 had goiters without hyperthyroidism. Three hundred and fifty of the first group were given preoperative treatment with antithyroid drugs. Three (0.21 per cent) of the 1,489 patients operated on for toxic diffuse goiter died, and 2 (0.17 per cent) of the 1,142 nontoxic patients operated on died. The operative risk, therefore, has been minimal in both groups. The disadvantages of prolonged preoperative medication with antithyroid drugs are as follows: occasional intolerance of these drugs, loss of time entailed by ineffective treatment, incomplete cure after a thyroidectomy performed too late, occasional auricular fibrillation and increased operative risk associated with the late stages of thyrotoxicosis and the problem of the relationship of prolonged antithyroid treatment to malignant degeneration of certain goiters. Collaboration of the physician and the surgeon is advisable before initiation of antithyroid treatment in certain cases.

New Symptomatic Drug for Parkinson's Syndrome.—Sigwald treated 106 patients with Parkinson's disease with 10-(2-diethylaminopropyl) phenothiazine hydrochloride (3356 RP). The initial daily dose varied from 0.05 Gm. to 0.20 Gm. The dose may be gradually increased to 0.15 and to 0.75 Gm., to be given in five divided doses. Twenty-three patients were treated for more than one year, 60 for more than six months and the remaining for three to six months. Forty of the 106 patients had Parkinson's disease of the senile or presenile type, and 66 had the postencephalitic type of the disease. Five patients were bedridden and akinetic, 79 were severely affected, 15 moderately and 7 slightly. Seventy-nine of the 106 patients who had been treated before with other synthetic antihistaminic drugs were intolerant or unresponsive to these drugs. The new drug has definite parasympathicolytic, sympathicolytic and spasmolytic properties. Ten patients experienced a nearly complete functional recovery. Good results were obtained in 35 patients and fair results in 37, with partial functional recovery and improvement in the symptoms. Temporary and functionally insufficient improvement took place in 21 patients. Treatment failed in 3 patients. These results were superior to those previously obtained in these patients with atropine, belladonna and scopolamine and superior to those obtained in 46 of the 79 patients treated with other synthetic antihistaminic drugs. The new drug had a definite effect on all the symptoms of the disease, predominantly on the rigidity, and a lesser effect on the tremor. It is suggested that the palliative action of the drug consists in a transsynaptic functional interruption affecting the extrapyramidal tract and particularly the cholinergic fibers.

57:833-848 (Sept. 24) 1949

*Chloromycetin in Treatment of Encephalitic Forms of Typhoid Fever. E. Benhamou, A. Albou, F. Destaing and A. Sorrel.—p. 833.
Diabetes Mellitus of Android Obese Women. J. Vague.—p. 835.
Prevention of Shock by Adding Procaine Hydrochloride to Intravenous Protein Solutions and Blood Transfusions. L. Leger, M. Lande and A. Beauvillain.—p. 837.

Chloramphenicol (Chloromycetin®) in Typhoid.—Benhamou and co-workers treated with chloramphenicol 5 patients with the cerebral type of typhoid and 3 patients with the usual type of typhoid. The patients with the common type of typhoid were given an initial dose of 2 to 4 Gm. of chloramphenicol followed by 0.25 Gm. of the drug every two hours until temperature was restored to normal. This was followed by 0.25 Gm. every four hours for three or four additional days, giving a total dose of 24 to 32 Gm. The temperature was restored to normal by lysis. There was a parallel improvement in all the other symptoms. Two intestinal hemorrhages requiring several blood transfusions occurred in 1 patient on the third day of the treatment. The patients with the cerebral type of typhoid required treatment with chloramphenicol for fifteen to twenty days with an initial dose of 4 to 6 Gm. followed by 0.50 Gm. of the drug every two hours, or combined treatment with chloramphenicol and 0.25 Gm. of aureomycin every four hours. Complete recovery took place in 4 patients, in 1 after a total dose of 60 Gm. of chloramphenicol and 7.50 Gm. of aureomycin had been administered. The fifth patient died after six days from an intestinal perforation which occurred after the temperature had been restored to normal. The dramatic results obtained with chloramphenicol in the cerebral type of typhoid suggest that high doses of the drug should be administered early and continued for prolonged periods in any grave case of the disease. Combined treatment with chloramphenicol and aureomycin is advisable.

Progrès Médical, Paris

77:417-448 (Oct. 10) 1949

*Thrombectomy in Phlebothrombosis. R. Leriche.—p. 419.
*Treatment of Tuberculosis with Para-Aminosalicylic Acid. J. Paraf. —p. 432.

Thrombectomy in Phlebothrombosis.—According to Leriche, thrombectomy followed by suture is the ideal operation in phlebothrombosis because it prevents embolism and preserves the integrity of the venous channel. Preoperative treatment with anticoagulants is not feasible in all patients. The method is not without risk and requires many more examinations of the blood than could be performed under present hospital conditions. Thrombectomy is indicated for early restoration of the permeability of the main trunk until a perfect thrombolytic agent will be available. Phlebography should be performed and treatment with anticoagulants be instituted as soon as the patient presents pain in the calf (Homan's sign), pain along the femoral vessels, edema or infarction. Heparin alone is required if the thrombosis remains limited to the calf. Thrombectomy should be performed if there is the slightest indication of femoral or iliac involvement. Ligation is reserved for exceptional cases.

Para-Aminosalicylic Acid in Tuberculosis.—Paraf reports on the effect of para-aminosalicylic acid in patients with pulmonary or pleural tuberculosis. Patients were given 20 to 24 Gm. of the drug by mouth daily in divided doses of 2 Gm. every two hours for one month. The course was repeated after an interval of several days. Para-aminosalicylic acid is indicated in recent progressive infections with a febrile course, with or without cavities, and particularly in patients who cannot tolerate streptomycin or who have become resistant to it. A series of thirty daily injections of 1 Gm. of streptomycin alternating with a one month course of daily administration of 25 Gm. of para-aminosalicylic acid by mouth is recommended to prevent streptomycin resistance. Roentgenologic clearing occurred within six weeks to three months. There was a drop in the temperature, increase in body weight, return of appetite, conversion of sputum and normal blood sedimentation rate. Para-aminosalicylic acid is indicated in primary infection in children and infants. Para-aminosalicylic acid was not effective in cases of long standing of fibrocaseous type and in the presence of old cavities. Highly satisfactory results were obtained with continuous intravenous drip of 30 to 50 Gm. of para-aminosalicylic acid in tuberculous meningitis and miliary tuberculosis. The intravenous administration of the drug may be combined with intraspinal injections of 1 to 3 cc. of a 10 per cent para-aminosalicylic acid–sodium chloride solution. Combined administration of streptomycin and para-aminosalicylic acid is advisable because of the gravity of the condition, but the specific value of para-aminosalicylic acid was proved by its effect in cases which had become resistant to streptomycin. Clinical, roentgenologic and ophthalmoscopic recovery occurred within fifteen days to three months in patients with miliary pulmonary tuberculosis in the absence of meningitic signs but with disseminated tubercles in the choroid and 0.40 to 0.60 Gm. albumin, 15 to 50 cell elements per cubic millimeter and tubercle bacilli in the cerebrospinal fluid. Intravenous injections of para-aminosalicylic acid were continued in these cases for three to five months and later were substituted by oral treatment with para-aminosalicylic acid. Clinical recovery with return of cerebrospinal fluid to normal occurred within four to six weeks of treatment in 3 of 6 patients with clinical signs of meningitis and positive cerebrospinal fluid. Clinical recovery took place in the remaining 3 patients, but the cerebrospinal fluid was not restored to normal.

Semaine des Hôpitaux, Paris

25:3295-3336 (Oct. 30) 1949. **Partial Index**

Pubiotomy. P. Lantuéjoul.—p. 3295.
Vitamin B_{12} and Antipernicious Anemia Factor. J. Cheymol.—p. 3305.
*Systematic Intraventricular Streptomycin Therapy for Tuberculous Meningitis. P. Nayrac, E. Laine, M. Fontan and others.—p. 3311.

Intraventricular Streptomycin for Tuberculous Meningitis.—Nayrac and co-workers treated 161 patients with tuberculous meningitis with streptomycin by intramuscular, intraspinal and intraventricular route. Administration of 2 Gm. of the drug followed by 1.5 Gm. daily by the intramuscular route proved indispensable in all cases. Intraspinal administration was discontinued because of considerable risks involved. Streptomycin hydrochloride 25 mg. (0.5 cc. of a solution obtained by dissolving 1 Gm. of streptomycin in 20 cc. of Ringer's solution) given by the intraventricular route once a week for twelve to sixteen weeks proved superior to the intraspinal route. It is the most logical treatment because it brings the drug to the ventricle, which are the site of the lesions. It offers considerable aid in diagnosis by facilitating the demonstration of the tubercle bacillus in the ventricular fluid, since the bacillus may be absent in the cerebrospinal fluid. The technic is simple and is not associated with pain. There were no contraindications and no untoward reactions. It results in pronounced relief from functional signs. Five of the 19 patients over 6 years of age with severe tuberculous meningitis treated by intramuscular and intraventricular route died or had recurrences, while the remaining 14 made a complete recovery. On the contrary, 4 of 5 patients treated by the intramuscular route alone died. These results induced the authors to practice the intraventricular method of administration systematically in all cases in which the diagnosis of tuberculous meningitis was established, instead of limiting it only to severe cases. The authors prefer streptomycin hydrochloride to streptomycin sulfate because of the risk of deafness associated with the latter.

Semana Médica, Buenos Aires

56:707-750 (Oct. 20) 1949. **Partial Index**

*Etiopathogenesis of Congenital Cardiopathies: Preliminary Report. J. C. Montanaro and R. A. Garrote.—p. 707.

Congenital Cardiopathies.—Montanaro and Garrote studied several patients with congenital cardiopathies or Laurence-Biedl's syndrome. They believe that these conditions have a common cause, namely, a heredofamiliar abnormality of the genes. The abnormality results in the establishment of diencephalic abnormalities in the embryo with lesions of the gray nuclei and the hypothalamic region. The heart lesion is caused by the diencephalic abnormality through an unknown biochemical mechanism. The authors extend this conception to the causation of other congenital abnormalities. They advise neurologic and psychiatric examinations of patients with congenital abnormalities of the heart and postmortem studies of the diencephalic centers in such persons.

Ugeskrift for Laeger, Copenhagen

111:1091-1114 (Oct. 6) 1949

Biologic Significance of Hyaluronic Acid and Hyaluronidase. Review. K. Schmith and V. Faber.—p. 1091.
*Determination of Salicylic Acid in Serum and Toxic Changes in Blood on Intensive Salicylic Acid Therapy. V. Faber and K. Schmith. —p. 1096.

Determination of Salicylic Acid in Serum and Toxic Changes in Blood on Intensive Salicylic Acid Therapy.—Intensive treatment with sodium salicylate in tablet form was given to 13 patients (8 adults, 5 children) with rheumatic fever. The salicylic acid concentration in the serum and the alkali reserve were measured twice weekly, the prothrombin level once or twice weekly. The salicylic acid concentration was determined by a modification of Coburn's method. Faber and Schmith state that during the treatment, which caused no significant symptoms, the average salicylic acid concentration in the serum was between 29 and 37 mg. per hundred cubic centimeters. The lowest prothrombin indexes were 41 and 45, the average value around 80. There was often a transient hypoprothrombinemia, but no hemorrhagic tendency. Increase in the serum salicylic acid concentration was accompanied with decrease in the alkali reserve. Simultaneously with a decided reduction in the alkali reserve more or less pronounced polypnea usually appeared. By simultaneous administration of sodium bicarbonate and salicylate the tendency to polypnea and reduction of the alkali reserve can be lessened, mainly because the intake of bicarbonate causes a more rapid elimination of salicylate through the kidneys, so that the salicylic acid concentration in the serum falls. The simultaneous administration of sodium bicarbonate and sodium salicylate is considered irrational. Caution is given against administration of large doses of salicylate in patients with uncompensated heart disease.

Book Notices

THE REVIEWS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES AND DO NOT REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED.

New and Nonofficial Remedies 1949: Containing Descriptions of the Articles Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1949. Issued Under the Direction and Supervision of the Council on Pharmacy and Chemistry of the American Medical Association. Cloth. Price, $3. Pp. 805. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C. 2; 2083 Guy St., Montreal, 1949.

This annual publication is essentially a textbook on the pharmacology of drugs selected for use in the contemporary physician's armamentarium, combined with a listing of available "acceptable" preparations containing them. The listing is the result of scientfic screening by the members and staff of the Council on Pharmacy and Chemistry as to justifiable therapeutic or prophylactic claims and checking of composition by the American Medical Association Chemical Laboratory. Over the years in which the book has been published, many drugs have been added as they have been developed and many omitted as not living up to their original promise or as having been replaced by more effective or less toxic agents.

Annual revisions keep the book up to date, and those of recent years have made the book more accessible and informative to physicians and other interested persons. In this edition the new chapter "Histamine Antagonizing Agents" offers a much needed critical delimitation of claims for products in this new and highly competitive field. The chapter on Local Anti-Infectives has been expanded by addition of a section on tests for antifungal agents. The penicillin monograph has been improved by an excellent reclassification of the various dosage forms in which this antibiotic is available. The chapter Testes has been critically revised, and the monograph Aminophylline has been rewritten.

Among the newly accepted preparations listed are, thenylene® hydrochloride (Abbott) and neohetramine® hydrochloride (Wyeth), both antihistaminics; lipo-adrenal cortex (Upjohn); Rocky Mountain spotted fever vaccine (Squibb); hycodan® bitartrate (Endo Products, Inc.), a brand of dihydrocodeinone bitartrate, and meonine® (Wyeth), a brand of DL-methionine.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1948, With the Comments That Have Appeared in The Journal. Cloth. Price, $2. Pp. 135, with 8 illustrations. American Medical Association, 535 North Dearborn St., Chicago 10, 1949.

This volume contains six substantial and informative reports covering the current status of therapy with various agents. One of these outlines the Red Cross program for determination of the place of human serum albumin in the treatment of patients having edema associated with renal diseases. Another details the usefulness of the new morphine derivative, metopon® hydrochloride (methyl dihydromorphinone hydrochloride). A group of three, reporting on organomercurial preparations, begins with a statement pointing out that as used these are bacteriostatic rather than bactericidal; questions are raised concerning their efficacy. Two supplemental reports, dealing with mercurochrome® (merbromin) and merthiolate® give evidence for these preparations but do not fully satisfy the question raised. The other status reports referred to are Protein and Amino Acid Preparations, a monograph, Streptomycin in the Treatment of Tuberculosis and Teropterin® and Diopterin® in the Treatment of Cancer, all valuable summaries or contributions in the subjects concerned.

Nine brief statements on protected and generic names recognized by the Council during the year attest the lively interest in drug nomenclature. A reprint current comment from THE JOURNAL, "More Silly Names for Penicillin Products," lists 25 such absurdities as Dairycillin, Hypercillin, Rectocillin and Vagicillin.

Three reports consign to the therapeutic scrap pile some groups of drugs that have outlived their usefulness or original promise, or have been replaced by better agents; Mercuric Compounds for use against Syphilis, Non-Official Salicylic Acid Derivatives and Antidysenteric Serums.

Only three reports of rejection appear: "Manogin"—Another "Bust Developer," Excessive Concentrations of Solutions Sodium Ascorbate and Alcohol-Dextrose and Dextrose-Vitamin Solutions for Infusion.

Tuberculosis of the Knee-Joint: An Exposition with Special Reference to Course and Treatment Based on Studies of the Literature and on an Analysis of a Material of Patients Observed Through Many Years. By Johannes Mortens. Translated from Danish by Axel Andersen. Paper. Price, 30 Danish crowns. Pp. 550, with illustrations. Ejnar Munksgaards Forlag, Nørregade 6, Copenhagen K: H. K. Lewis & Co., Ltd., 136 Gower St., London, W.C. 1, 1948.

This monograph is an astounding work and is based on a most intensive study of the author's series of 181 cases and a comprehensive perusal of literature on the subject. The author has utilized his material with a measure of care and accuracy to which few other monographs can lay title.

The book consists of four major chapters: The first deals with pathogenesis, pathology, course and development of the disease. It contains some interesting details, such as the explanation of universal miliary tuberculosis and primary tendency to multiple localization on the basis of bacillemia. On the same grounds, the author explains the latency period and ability of trauma to activate and release tuberculous foci. For this, there is ample evidence in the author's own clinical material. Thus, the author finds himself in accordance with the view of Johannes Meyer, Broca and Sven Johansson, in corroboration of the systemic nature of the disease and especially in explanation of the simultaneity of the diverse tuberculous eruption. In the pathologic discussion, there is nothing particularly new except the mention of sequestral foci and the preponderance of the metaphyseal over the epiphyseal foci in children, and vice versa in adults. The contrast between the slow or creeping and the more rapid or sequestering type of necrosis between children and adults is duly mentioned. "Kissing sequestra," while nothing new, are demonstrated by a number of cases. The presentation of the pathologic changes is complete and clear, particularly the paragraphs which deal with contracture deformities and growth changes.

The second chapter is devoted to symptomatology and to diagnosis. It is particularly commendable that the early subjective signs are given close attention. The author's remarks on the interpretation of the tuberculin reaction seem especially appropriate. So also is his consideration of the chronic gonitis of uncertain origin. This type of condition, not due to pyogenic or tuberculous infection, is assigned to the group of chronic, nonspecific arthritides, on the basis of pathologic findings established by others, such as Sundt and Ghormley. Also of special interest is the author's appraisal of the value of the clinical diagnosis. He mentions Ghormley's margin of error as 38 per cent, which tallies with Milgram's of 39 per cent. He uses these data as an argument for biopsy when the demonstration of tubercle bacilli and guinea pig test have not given unequivocal information. At the same time, the author considers it unreasonable to demand biopsy in all cases and at all ages. He has a comparatively high percentage of unquestionable diagnoses—112, in 181 cases.

Chapter 3 is devoted to the course of tuberculosis. The conclusions essentially conform to the commonly accepted opinions, particularly Kremer and Wiese's classification of the granulating and caseous forms, rather than the dubious and more artificial distinction in hydrarthrosis, fungus and pyarthrosis, which he rightly considers as merely transitional stages. He discusses the course according to what he calls the marginal destruction type and the deep destruction type. The ultimate outcome is analyzed on the basis of these types. He distinguishes, consequently, the fibrous healing without injury to the articular surface in children, versus a rapid and complete reduction of the articular surface, and the severe marginal destruction. His point that the course cannot be well established in adults because most of them have undergone resection or amputation in the course of the disease is well taken.

The fourth chapter deals with treatment. While the description of treatment methods follows more or less conventional lines, there are also brought out a number of interesting points: The early history of the treatment of the knee in the nineteenth century is interesting; particularly attractive is the presentation of the modern treatment since 1900 in the different countries, e. g., resection as it prevailed over conservative treatment or heliotherapy in Germany, the more cautious attitude of the French regarding resection, under the influence of heliotherapy, the British conservatism, especially for children, in this country the change from conservatism to radicalism under the impact of the teachings of Hibbs, later tempered by restrictions regarding the age of the patient and the duration and stage of the disease, and in the Scandinavian countries, under the influence of Waldenstrom, conservatism in children and in all synovial cases. Mortens' own opinion is that resection may be performed from the age of 9 to 10 without any appreciable postoperative deformity or contracture, but tuberculosis of the knee in children should always be treated conservatively. Early resection, from 9 years on, is indicated in cases of considerable surface destruction, while resection should be postponed to 13 or 14 years in cases of deep destruction. In adults, he restricts conservatism to the mildest cases, where the dreaded disease is strictly localized in the synovia.

There is, on the whole, little to which one can take exception in the entire treatise. Most of the author's views are in harmony with the generally accepted opinions, at least in this country and in Great Britain. The work is extremely thorough; it covers a minute and painstaking analysis of the author's cases, and there is appended not less than 548 references. The work represents an excellent and most illuminating study on this difficult and somewhat controversial subject; it is recommended for serious study to anyone interested in the surgery of the skeletal system and particularly in skeletal tuberculosis.

Bridges' Dietetics for the Clinician. Edited by Harry J. Johnson, M.D., F.A.C.P., Assistant Attending Physician to the Hospital, Associate Attending Physician to the Dispensary, Chief of the Nutrition Clinic, New York Post Graduate Hospital, New York. Fifth edition. Cloth. Price, $12. Pp. 898. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1949.

The fifth edition of this useful book on dietary management retains the general form of previous editions with some sections extensively revised and others largely unchanged. Part I deals with general considerations of digestion and with the classification, structure and constituents of foods. In one chapter, foods which have high and low concentrations of specific nutrient factors, e. g., cholesterol, iron, purines and individual vitamins, are listed in tabular form. This section has been revised in accordance with recent knowledge of the distribution of nutrients in foods and is extremely useful. It is regrettable that the chapter on vitamins has not also been subjected to considerable revision. While some changes have been made, most of the references are to studies conducted prior to 1940. A chapter on supplementary methods of feeding might be improved by the addition of a section on parenteral nutrient therapy.

Part II of this book deals with the dietetic management of diseases of adults. Diseases are arranged in alphabetic order and are discussed by various specialists who comprise the 27 contributors to this volume. The indications and rationale for specific dietotherapy are outlined, and numerous diets, with menu plans, are given in detail. This section should be particularly useful to both the practicing physician and the dietitian.

One of the most valuable portions of the book is the appendix, which constitutes about one third of the volume. This section includes height-weight tables, recommended dietary allowances, a glossary of vitamin terms, tables of the nutritive and caloric value of foods and of their acidity, water, mineral and vitamin content. The food tables, which have been simplified, augmented and brought up to date, contain a wide variety of common foods and a number of proprietary preparations.

This book is highly recommended as a practical aid and reference in planning therapeutic diets in a wide range of diseases.

How a National Health Program Would Serve the South. Paper. Pp. 24. Committee on Research in Medical Economics, Inc., 1790 Broadway, New York 19, 1949.

The report of Mr. Davis and his committee contains the usual disparaging remarks concerning unnecessary death, misery and ill health, draft rejections, inadequate hospital facilities and rural health needs, pointing out that these problems are particularly acute in the Southern states.

Mr. Davis attributes the health problem of the South to low income and inability to pay. The author's solution, therefore, is to provide individuals and families with purchasing power for medical care by National Health Insurance—"a national solution which would particularly benefit low income areas in the nation."

Part II of the report describes the special benefits for the South to be derived from President Truman's program for National Health Insurance and Aid to the States to increase and improve medical manpower, hospitals, research, public health services and professional education.

Part III contains a study of 12 Southern states, showing how each ranks on several health measures, comparing health services and records with those of New York, Minnesota and Washington and giving the statistics on medical care available in rural areas.

This is just one more story of "something for nothing." In addition it paints a black picture of conditions in the South, particularly the rural South. It attributes the problem to inability to pay and does not mention housing, the degree of literacy of the people involved, and climatic and geographic factors. The South has been dealing for many years with problems in education, housing and agriculture, but the report ignores the implications of such factors.

The most glaring omission in this report is its failure to credit the efforts and achievements of at least half the states. It mentions hospital construction in Mississippi only, but says nothing of the North Carolina Medical Care Commission and its comprehensive program. It does not mention the Virginia Council on Health and Medical Care and improvements effected through it, or the Rural Health Improvement Association sponsored by the Tennessee Farm Bureau Federation. It also overlooks the organized activities for health and medical care in South Carolina, Texas, Kentucky and Alabama. These states are not as far behind the times as the report indicates and many are proving what can be achieved through voluntary interest and cooperation.

Vision: Its Development in Infant and Child. By Arnold Gesell, M.D., Frances L. Ilg, M.D., and Glenna E. Bullis. Assisted by Vivienne Ilg, O.D., and G. N. Getman, O.D. Cloth. $6.50. Pp. 329, with 56 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33rd St., New York 16, 1949.

This volume covers intensive studies of infants and young children over a period of years at the Yale Clinic of Child Development. It represents the most complete clinical study of the various stages of the development of vision ever undertaken. The conclusions drawn from the large number of children examined and studied represent an advance in the knowledge of the subject particularly in relation to the total action system of the child, but many questions remain unanswered. The authors have shown, perhaps wisely, a tendency to refrain from overemphasis on theory and to limit description largely to the results of observation.

After an introduction in which there is a discussion of the eyes of today and tomorrow, orientation of the study, the evolution of the human action system and the motor basis of vision, the book is divided into three parts. The first concerns the growing action system in relation to the genesis of vision and its development from infancy to the age of 10 years. Emphasis is laid on the relation of vision to other activities as a part of the general pattern of development. This is done in considerable detail, so that the study should be of interest not only to pediatricians but to intelligent parents as well. The second part of the work is devoted to a study of developmental optics. The interpretation of retinoscopic findings, including "dulness" and "brightness" of the reflex, might be open to question, since the factors of accommodative spasm and fundus pigmentation have not been adequately considered and

apparently no attempt was made to determine accurately refractive errors with a cycloplegic. Of particular interest is the chapter on amentia and the behavior of the blind child. The final portion of the book is devoted to developmental appraisal, including an appendix which assembles "visual behavior patterns in systematic ontogenetic sequence," under the headings of eye-hand coordination, postural orientation, fixation, retinal reflex and projection. This furnishes a handy summary for ready reference.

This volume is recommended to anyone interested in the development of vision in the child. It offers a real contribution to the undertaking of this important subject.

Social Security Services in New Zealand: What We May Learn From Them. By E. W. Maples, LL.D. Paper. Pp. 34. The Author: 59 Bodenham Road, Hereford, England; Oxford University Press, Amen House, Warwick Sq., London, E.C. 4, 1949.

The author writes on the basis of an eight week visit to New Zealand to study the social security services. Much of his report is written in the form of comparison to the British system, and the pamphlet provides an interesting and informative over-all survey.

In tracing the history and development of the medical services program in New Zealand, Mr. Maples gives particular attention to the stand of the British Medical Association, explaining its objections, criticisms and suggestions.

On the whole, he finds the New Zealand program unsatisfactory and shows evidence that ethical standards and quality of medical care have been seriously lowered. The method of paying doctors is such that general practice is the only profitable area, and there is absolutely no inducement to become a specialist, professor or member of a hospital staff.

It is simple for patients, doctors and pharmacists to exploit the system, and there has been a strong tendency to take advantage of this situation. The program has been expensive, and costs will continue to increase year by year.

Mr. Maples tells of the Cleary Committee set up in 1947 to investigate and report on the difficulties of the system and recommend reforms. He agrees with most of the proposed changes but indicates that the British plan will be superior to that of New Zealand in many respects.

The author considers environmental and other influencing factors. He has visited the cities as well as smaller and rural areas, and has consulted with government, professional and lay persons. His study appears to have been objective and comprehensive, although the pamphlet is too brief to give a complete and detailed report.

Atlas of Surgical Operations. By Elliott C. Cutler and Robert M. Zollinger, Professor and Chairman of the Department of Surgery, Ohio State University College of Medicine, Columbus. Second edition. Cloth. $9. Pp. 225, with 106 plates by Mildred B. Codding, A.B., M.A. The Macmillan Company, 60 5th Ave., New York 11, 1949.

This book is, as the name implies, an atlas of surgical operations that are in common use at the present time. The procedures are well chosen, and the excellent drawings by Miss Codding illustrate admirably and in great detail the various steps in the operation. The book should prove to be of great value to house officers securing surgical training and to the general surgeon who is called on to perform an operation that he has not done for some time. Directions regarding preoperative and postoperative care accompany the drawings and are simple, lucid and well chosen. The book is strongly recommended for the library of the modern surgeon.

Confrontations radio-anatomo-cliniques. Fascicule III. Publiées sous la direction de M. Chiray, R. A. Gutmann et J. Sénèque. Paper. Price, 1,000 francs. Pp. 79, with 150 illustrations. Gaston Doin & Cie, 8 Place de l'Odeon, Paris 6e; Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1949.

The highly interesting cases presented and the manner of preparation of the clinical material won warm appreciation from surgeons, radiologists, gastroenterologists and other clinicians for the first two volumes of this publication.

The present volume continues the high interest and excellence of illustrative material. The majority of cases represent classic and atypical, easy and difficult problems. Each case is briefly described. Considerable importance is given the radiographic evidence which has contributed to the diagnosis or which has led into error, followed by brief operative detail and microphotographs of the corresponding specimen. Gastroenterology seems to be the favorite subject in these case presentations, but the other branches are not neglected. This is really an atlas of clinical radiology.

Iron Metabolism and Its Clinical Significance. By A. Vannotti, M.D., Director of the Medical Polyclinic and Professor of Internal Medicine in the University of Lausanne, and A. Delachaux, M.D., Lector of the Medical Polyclinic of the University of Lausanne. Translated [from German] by Erwin Pulay, M.D. Cloth. $6.50. Pp. 267, with 11 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1949.

This book was written originally in 1942 and translated from the German in 1949, when it was recast and supplemented. It covers the results of investigations carried out by the authors and deals largely with serum iron. They give special emphasis to the separation of the serum iron into four fractions and review the early work of Barkan, Heilmeyer and Starkenstein. This book has little value for the clinicians but may be of some interest to investigators specializing in iron metabolism.

Numerous inconsistencies and lack of references to early significant work appear in the introductory chapter on iron metabolism. Figures are presented which do not designate units for the values given, and the bibliography contains misspelled words and incomplete references.

Facts pertaining to iron metabolism can be obtained more readily from other books, but it is interesting to obtain the viewpoint of these workers and, as the authors point out, this book may help establish closer contacts with scientists interested in this field.

Varices: Su tratamiento basadoen la flebergrafía. Por el Dr. F. Martorell, jefe de la Sección de cirugía vascular del Instituto policlínico de Barcelona. Half-cloth. Pp. 140, with 118 illustrations. Editorial Labor, S. A., Barcelona, 1946.

This is a beautifully printed and illustrated monograph on the value of phlebography in the rational treatment of varicose veins. This work was published in 1946, and some of the more recent developments in this field, such as the revival of the stripping operation and the use of deep venous divisions in the postphlebitic types of varicosities, have not been included. However, there are beautiful phlebograms and diagrams of the most common types of valvular insufficiency in the lower extremities. Perhaps the American reader might object to the use of colloidal thorium dioxide or 30 per cent sodium iodide for the visualization of vessels. Neither of these solutions has found favor among workers in this field. It is also questionable whether much of the information derived from these phlebograms could not be obtained by methods of physical examination. Nevertheless, the accumulated material and the clarity of presentation are impressive. For those interested in the pathogenesis and treatment of varicose veins this monograph will be most stimulating.

Malnutrition and Starvation in Western Netherlands September 1944-July 1945. Part I. Part II: Appendices. [Editorial Committee: Netherlands, Dr. G. C. E. Burger (Chairman); U. S. A. and Canada, Lieut. Col. H. R. Sandstead; Great Britain, Sir J. C. Dummond]. Boards. Pp. 187; 299, with illustrations. General State Printing Office, The Hague, 1948.

This report will be distributed by the U. S. Public Health Service to medical libraries, health departments and research workers in the field of nutrition. These two volumes constitute a report on the nutritional status of the people of Western Holland at the war's end. The first volume contains the text of the report, while the second contains the more detailed tabulated data on which the report is based. While the report does not contain all the information that might be desired, it is nonetheless a valuable document of interest to medical research workers, nutritionists, medical students and all who are or may be concerned with the problem of dealing with or preventing mass starvation, including the civilian affairs division of the military services and state departments and of national and state departments of health. Americans who took an active part in the preparation of the report include Drs. V. P. Sydenstricker, F. J. Stare, C. E. French, Chas. Leach and M. B. Corlette.

The report deals with the nutritional status of the civilians in Western Holland before and during occupation and after

liberation, and also describes organization and preparations for relief, survey methods, treatment and pathophysiologic aspects of starvation. It emphasizes the importance of putting a starving person as quickly as possible on a diet of high energy value and high protein content. Patients with rare exceptions could swallow and digest relatively large quantities of simple food mixtures, based chiefly on the use of separated milk powder. It was proved that the predigested foods of the protein hydrolysate type are not essential for resuscitation of patients in the last stages of exhaustion from starvation.

It is easy to understand why the report ends as it does, with a plea that such human suffering as these workers saw in Holland be outlawed. The following quotation is from the end of the report and constitutes special recommendation: "The Editorial Committee wishes to record its considered opinion that there is no justification for the ruthless sacrifice of a civilian population in such circumstances and that the United Nations should devise a Convention of international scope of which the object would be to protect civilians subjected to an occupying power from suffering grave injury to health as a result of inadequate nourishment."

Natural Products Related to Phenanthrene. By Louis F. Fieser and Mary Fieser, Department of Chemistry, Harvard University, Cambridge, Mass. [American Chemical Society Monograph No. 70.] Third edition of the monograph previously entitled Chemistry of Natural Products Related to Phenanthrene, by L. F. Fieser. Cloth. Price, $10. Pp. 704 with illustrations. Reinhold Publishing Corporation, 330 W. 42d St., New York 18, 1949.

It is a curious fact that many hormones, sterols and bile acids which are so important to health and well-being are related chemically to the rather simple coal tar hydrocarbon, phenanthrene. This book sums up present knowledge of these substances and includes chapters on cardiac glycosides, morphine and related alkaloids, saponins, steroid alkaloids and steroid metabolism. Although written primarily for the organic chemist, the material is presented in such a manner that it will be of considerable interest to physicians and others who are primarily concerned with physiologic applications.

The study of hormones from the chemical point of view, although exceedingly difficult, has made great progress in the last two decades and is now in a state of feverish activity. For instance, the synthesis of cortisone (compound E) is described in detail, and a discussion of its physiologic activity and comparison with other adrenal cortical hormones is given. These discussions are liberally annotated with references to the original reports.

Professor Fieser's book is a major contribution, as it correlates the work of many scientists and enables the reader to acquire the background in these intriguing fields which through personal searching might take many years.

Public Health Bacteriology and Parasitology. By C. G. Booker, M.D., Ch.B., D.P.H., Railway Health Officer, Deputy Chief Health Officer, Union of South Africa. Cloth. 35s. Pp. 234, with 108 illustrations. Johannesburg, 1949.

This book was published primarily as an elementary textbook and guide for public health field workers employed by the South African Railway Administration, to facilitate their systematic classification of the "more important bacteria, protozoa, helminths, molluscs, arthropods and vertebrates which are either the direct causative agents of disease or which serve as vectors, hosts or reservoirs of infection in South Africa." It was not intended for nor is it adequate for use as, an authoritative manual for positive identification of species.

The section on public health bacteriology touches on the fundamental classification of micro-organisms, their habitats and pathogenicity. The bacteriologic nomenclature employed is not modern. Fundamentals of immunology are also included in this section of 96 pages.

The larger section on public health parasitology reflects the importance of protozoa, helminths, insects and rodents as agents and vectors of disease in that area. The author has included descriptions of a few species which are not naturally found in South Africa but "which may be introduced through modern systems of travel."

The illustrations, photographs and charts are well executed.

Chirurgie réparatrice. Par R. Merle d'Aubigné. Avec la collaboration de J. Cauchoix, et al. Paper. Pp. 348, with 51 illustrations. L'Expansion scientifique française, 23 rue du Cherche Midi, Paris, 6e, 1949.

The book is based on the work performed at the National Center for Surgical Repair and Rehabilitation at Surenes (near Paris) from November 1944 to April 1949. It reflects the best opinion, procedure and technic of the French school of orthopedic and reparative surgery.

The author, who is a leading surgeon in France and one of the leading men of Europe, has had extensive military and civilian experience. His basic training was excellent. He is a surgeon first, last and always. He is a "sharp-dissection" surgeon. He is fearless, painstaking and tireless. Personal observation of him in action, performing every type of procedure described and illustrated in this book, vouches for his qualifications, industry, initiative and veracity.

He discusses lumbosacral arthrodesis in the treatment of lumbar sciaticas. He reports on 78 patients with sciatica and on others with spondylolisthesis, disk lesions and lumbago. Among the subjects discussed are spinal fusion, pseudarthrosis, loss of substance and medullary nailing for diaphyseal fractures with either malalinement or nonunion. He describes the treatment of chronic traumatic osteomyelitis, preganglionic sympathectomy in the treatment of post-traumatic pain, painful stumps and causalgia, treatment of traumatic arterial aneurysm and arteriovenous fistulas, treatment of loss of substance of skin, wounds of median nerve and tendon transplant in the treatment of post-traumatic radial paralysis. The indications and technic for tibiotarsal arthrodesis, postmarginal fracture with vicious consolidation, arthrodesis of the wrist and operative treatment of the stiff knee are discussed, as well as treatment of war wounds of peripheral nerves, surgical treatment of varicose ulcers, protein deficiencies and their treatment in surgical repair, protein metabolism in the anemia of burned persons and reanimation and traumatology and physical rehabilitation.

This I Do Believe. By David E. Lilienthal. Cloth. $2.50. Pp. 208. Harper & Brothers, Publishers, 49 E. 33rd St., New York 16, 1949.

This group of essays is of great interest, spelling out the reasons for faith in democracy as those reasons have been evolved by one of our most distinguished and perceptive public servants. Reading this book will be good for those troubled by the many alarms and fears of present times, for those who have lost sight of the fundamental nature of the democratic principles which have made America. Implicit in most of these essays is the basic belief that the opportunity is more important than matter.

Particularly relevant in these days of uncertainty are the few pages dedicated to the thesis that an informed public may control its own destiny. This, long apparent to doctors concerned with the medical and social welfare of the community, has been vividly expressed here.

Many of the examples Mr. Lilienthal uses in making his points are drawn from his experience with the Tennessee Valley Authority and the Atomic Energy Commission. Lilienthal points up clearly the dangers that may lead to the ultimate catastrophe—a nonmoral world.

Man and This Mysterious Universe. By Brynjolf Bjorset. Cloth. $3.75. Pp. 174. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1949.

This book apparently was inspired by the late Indian musician and scholar Inayat Khan. It contains many references to the controversial views of Dr. Oscar Brunler. The main tenet, so far as can be determined, is that all human behavior is based on "vibrations." A typical quote follows: "There are the seats of his physical senses, eyes, ears, nose, tongue, and the centers of feeling, each of them tuned to the particular kind of vibrations which feed them and give them worry or delight. Food brings into the body vibrations which sustain and quicken the vibrations of tissue, blood, brain matter and nervous system —or break them down if this food is not suited to this particular individual" (page 27). Because of his training the average physician will find the philosophy presented difficult to follow and unconvincing.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

HIGH BLOOD PRESSURE

To the Editor:—**Are you in agreement with an article published in *Readers Digest*, August 1949, entitled, "High Blood Pressure? Don't Be Alarmed," written by Joseph Weitzenkour? In this article, which the author states has the complete approval of the medical director of the American Heart Association, are found statements such as these: "Once you have high blood pressure, it doesn't matter whether your blood pressure is up a little bit or a whole lot." "You are no worse off with a pressure of 250/150 than with a pressure of 160/100; you're not more likely to get a stroke or an enlarged heart or any of the other damage associated with hypertension and your living chances are just as good as any hypertensive's." "The degree of hypertension has nothing to do with anything."**

J. Howard Baker Jr., M.D., Eufaula, Okla.

ANSWER.—Authorities on hypertension do not agree with the quoted statements in the query. Such generalizations are false, unwarranted, misleading and dangerous. As is frequently the case in articles prepared by persons lacking a thorough knowledge of the subject, omissions may be more misleading than some of the statements.

The immediate and long term prognosis of the hypertensive person are two separate problems. Several factors affect the prognosis: (1) the etiologic picture of the individual case, (2) the age of the patient, (3) the rate of the progression of the disease (determination of which requires knowledge of duration), (4) the stage reached in its pathogenesis (extent of irreparable, irreversible arteriosclerotic change), (5) the character and extent of complications, including the cardiac and renal reserve, and (6) the cooperation of the patient. All these elements are significant. (Hypertensive Arterial Disease and Hypotension in Geriatric Medicine, edited by E. J. Stieglitz, Philadelphia, ed. 2, W. B. Saunders Company, 1949, chap. 30).

Hypertensive disease varies in intensity and in rate of progression. Day by day or hour by hour fluctuations are not profoundly significant except as they reveal the degree of spasticity in contrast to arteriosclerotic constriction and may bring to light information on the etiologic factors inducing arteriolar hypertonia. In instances of slowly progressive hypertension which may have continued for many years, moderate hypertension may be physiologically necessary and therefore desirable, but levels of 250/150 are dangerous. The age of onset of the disorder is significant; the later in life hypertensive disease arises, the more it tends to be benign and slow in its progression. The level of the arterial tension, though only one of several factors determining the prognosis, is nevertheless significant.

EFFECTS OF ALCOHOL

To the Editor:—**Please advise whether alcohol up to say 3 ounces (88 cc.) is considered a stimulant? Would more than that amount be considered a depressant?**

W. J. Singleton, M.D., LaCrosse, Kan.

ANSWER.—The effect of alcohol on the various body systems should be viewed separately. Alcohol in the mouth increases salivation, but so does lemon juice. In the stomach alcohol increases the secretion of gastric juice, but concentrations over 5 per cent retard digestion. The production of pancreatic juice is inhibited by concentrations over 2 per cent. The cutaneous blood vessels are dilated by alcohol, producing the well known flushing of the face. The feeling of warmth after taking alcohol is deceptive, because this feeling is associated with rapid heat loss. The heart beat occasionally is accelerated by alcohol, although the same effect may be obtained by merely holding 50 per cent alcohol in the mouth. Small amounts of alcohol, up to 0.1 per cent in the blood, increase respiratory movements but amounts over 0.2 per cent are followed by some inhibition of respiration. Again the stimulating effect of alcohol is in doubt, since the carbon dioxide output is decreased during the stage of increased respiratory activity.

The most important action of alcohol is on the nervous system. Small doses of alcohol appear to have a stimulating action by giving the drinker a feeling of well-being and increased self confidence, but unfortunately with a loss of judgment and the ability of self criticism. The apparent stimulation is the result of the narcotic action of alcohol on the inhibitions. This depressant action involves first of all the higher centers of the brain, which are responsible for acquiescence to the habits of civilization. The dulling of the feeling of responsibility allows the more primitive cerebral functions to dominate. The fallacy of the stimulating effect of alcohol is greatly enhanced by the drinker who is convinced that he is performing better when he is under the influence. Bogen has aptly compared this apparent stimulation to a car on a hillside. Alcohol releases the brakes but does not cause the car to run better.

One of the pioneers in correctly evaluating the action of alcohol is O. Schmiedeberg, whose thesis concerning its depressant action was published in the first edition of *Grundriss der Arzneimittellehre* (Leipzig, F. C. W. Vogel, 1883). In a later publication (*Grundriss der Pharmakologie* in Bezug auf Arzneimittellehre und Toxikologie, Leipzig, F. C. W. Vogel, 1902) he writes: "The subjective and objective manifestations are usually attributed to a stimulating effect of the alcohol. One refers to the manifestations which we observe under these conditions, namely to certain exaltations of the psychic functions resulting in loud and profuse speech, and vivacious acts, also to accelerated pulse rate, engorgement and flushing of the body surface and the face, and a sensation of increased warmth. However, a closer consideration of these manifestations shows that they are the results of a beginning paralysis of certain parts of the brain. The idea that alcohol acts as a stimulant to the nervous system is no longer held in pharmacological circles. In the psychic sphere there is first lost the finer grades of attention, judgment, reflection, and ability to comprehend. This serves to explain the typical behavior of persons under the influence of alcoholic drinks. The soldier becomes more courageous since he observes the danger less, and reflects upon it less. The speaker is not tormented and influenced by the proximity of the public; he, therefore, speaks freer and with more animation. One's self-appraisal rises greatly. Often one is astounded at the ease with which he expresses his thoughts and with the keenness of his judgment in matters which are beyond his mental sphere when sober, and is later ashamed of this delusion. The drunken individual attributes to himself great muscular strength and wastes this through unaccustomed and useless exhibitions of strength without thinking of the harm which may ensue, while the sober person willingly spares his strength."

PREPARATION OF HANDS FOR SURGERY

To the Editor:—**Please send me data on (1) preparation of the hands for surgery; (2) effectiveness of methods of preparation of the hands for surgery; (3) any apparatus or equipment that may have been used in the preparation of the hands for surgery, and (4) effects of difference in time spent in preparing the hands for surgery.**

Ralls M. Coston, M.D., Birmingham, Ala.

ANSWER.—Investigators have been working for years on improving the germicidal properties of soap. Most of these experiments have terminated unsuccessfully, because soap tends to destroy the action of any incorporated germicidal compound. Within the past few years, however, several preparations have been investigated which maintain their antiseptic qualities when incorporated into soap or a detergent. The most successful of the compounds used to date is hexachlorophene (G-11) in either 2 or 3 per cent concentration.

The scrub brush is still advocated for the first scrub of the day, since it aids in the removal of street dirt and desquamating epithelium. A two to three minute hand preparation using the antiseptic compounds has been found to give colony counts at least as low as those found following a ten minute scrub with unmodified soap or detergent. However, successful use of the hexachlorophene preparations is dependent on routine and repeated use of the cleansing agent. Price and Bonnett have shown to their satisfaction that single applications of the modified cleansing agents are no more effective than unmodified soap or detergent. (Price, P. B., and Bonnett, A.: The Antibacterial Effects of G-5, G-11 and A-151 with Special Reference to Their Use in the Production of a Germicidal Soap, *Surgery* **24**:542, 1948.)

More important than the number of bacteria present at the conclusion of the hand preparation is the number of viable bacteria present on the hands at the end of the operation. Clark, Lockwood and Lewit have shown that use of a 2 per cent concentration of hexachlorophene gives a decided reduction in bacteria at the end of a surgical procedure compared with an increase following the use of soap alone. (Clark, D. G. C.; Lockwood, J. S., and Lewit, E.: 2,"8 Dihydroxy-3,5,6-3',5'6' Hexachlorodiphenylmethane [G-11] as an Antiseptic for Use in Surgical Scrubbing, *Surgery* **22**:360, 1947.)

Freeman and Young have found pHisoderm® (a detergent cream composed of a sulfonated ether, petroleum, lactic acid and wool fat cholesterols) combined with 3 per cent hexachlorophene to be particularly efficacious. In actual clinical trial they were able to achieve pronounced reductions in postoperative infections.

(Freeman, B. S., and Young, T. K. Jr.: Clinical Study of the Use of a Synthetic Detergent [pHisoderm] Combined with G-11 for Disinfection of the Skin, *Surgery* **25**:897, June, 1949.)

A low rate of infection depends as much on proper preparation of the operative site as on preparation of the surgeon's hands, and the same modified cleansing agents are being utilized in preparation of the patient's skin.

Each soap and detergent containing hexachlorophene, now commercially available, has its own peculiarities; the suggestions of the manufacturer should be carefully followed in its use.

IMPAIRED RENAL FUNCTION AND PREGNANCY

To the Editor:—A white woman aged 29 was admitted to the hospital with edema of the face. Three weeks before admission she had had generalized aching, a slight nasal discharge and elevation of temperature, for which she took acetylsalicylic acid. Within two or three days she resumed her activities as a housewife and school teacher. Five days before admission she noticed fulness of the face on awakening, but this subsided during the day. The next morning it was again observed and was thought to be more pronounced. The edema increased and involved the entire body, but chiefly the face and upper extremities. She had one pregnancy terminating in a normal male child now 4 years of age. Her blood pressure was 140 systolic and 92 diastolic. There was a waxy appearance to the complexion and edema of the face and upper extremities; there was some pitting edema over the lumbosacral region and to a less extent of the lower extremities. Ophthalmoscopic examination, and the ears, nose and throat, revealed essentially normal conditions. The heart is not enlarged. The uterus is small, in the anterior position, and there are no palpable adnexal masses or tenderness. Rectal examination does not reveal anything unusual. The red blood cell count is 3,940,000, the white cell count 5,200 with 73 per cent polymorphonuclear cells, 2 per cent eosinophils and 25 per cent lymphocytes. The reaction to the Mazzini flocculation test was negative. Other laboratory data were within normal limits except for low specific gravity, trace of albumin and occasional red blood cells and granular casts in urine. She was discharged two weeks after admission. Since that time the urine has been free of red blood cells, casts and albumin; however, the specific gravity has remained low. The patient is without complaints, but it appears that she has some impairment in renal function. She desires another pregnancy. Could this patient go through a well supervised pregnancy without developing complications due to this impaired kidney function? M.D., North Carolina.

ANSWER.—This patient may safely undertake another pregnancy, but of course, her urine, blood chemistry, blood pressure and weight will have to be checked at frequent intervals. A second pregnancy should not damage her kidneys any further or shorten her life.

MENTAL DEFICIENCY AND Rh INCOMPATIBILITY

To the Editor:—Is there an increased incidence of mental deficiency in children as a result of Rh incompatibility? M.D., New York.

ANSWER.—The relationship of Rh incompatibility to mental deficiency is as follows: If a sensitized Rh-negative woman gives birth to an Rh-positive baby that baby will almost invariably be erythroblastotic. Among erythroblastotic babies treated conservatively with simple blood transfusions who survive, as many as 10 to 30 per cent subsequently exhibit neurologic sequelae. In mental institutions, however, such cases are rarely encountered and account for only about 5 per cent of the cases of so-called undifferentiated mental deficiency. Since the incidence of Rh-negative women is high (15 per cent among Caucasians) it may seem strange that these cases are so rare; the explanation is that only a small percentage of the Rh-negative women become sensitized, so that the incidence of erythroblastosis is only 1 in about 300 births. Recent work has shown that if erythroblastotic babies are treated immediately after birth by exchange transfusion, instead of by simple transfusions, not only will the survival rate be higher but neurologic sequelae will also be prevented (Wiener, A. S.; Wexler, I. B., and Gibbel, N. F.: Does Exchange Transfusion Prevent Neurologic Sequelae of Erythroblastosis Fetalis? J. A. M. A. **141**:280 [Sept. 24] 1949).

CYTOCHROME C

To the Editor:—What is the present status of the use of cytochrome C in the treatment of senile dementia? M.D., Arizona.

ANSWER.—Cytochrome C, an important respiratory enzyme occurring in plant and animal tissue, has been the subject of numerous experimental investigations and clinical trials in a variety of disorders.

Satisfactory evidence of the therapeutic value of cytochrome C in senile dementia and related disorders appears to be lacking, although it may have been tried on the basis that the enzyme might improve oxygenation of the brain tissue. As shown by several workers, this action appears doubtful.

TREATMENT OF FILARIASIS

To the Editor:—A man from India who has filaria has been treated for a long time without success with the arsenic preparations. He has heard that a new treatment is being given in the United States. Please advise me where to get the new drug.

Karel Van Gelder, M.D., Portchester, N. Y.

ANSWER.—Some recent experimental treatments for filariasis have been reported to be efficacious by some workers, but sufficient data are not yet available for approval of these products. The majority of reports on medicines which are available show a general preference for 1-diethylcarbamyl-4-methylpiperazine dihydrogen citrate. It can be purchased as hetrazan® from Lederle Laboratories, Inc., 30 Rockefeller Plaza, New York City.

Differences have been reported in toxic reactions and dosage in the treatment of infection with various species of filaria, but results in infections due to Wuchereria bancrofti are generally satisfactory. There is a difference in systemic reactions to the drug in asymptomatic cases and those with certain definite clinical symptoms at the time of treatment. During the early period of treatment in some cases, temporary exacerbations of clinical symptoms occur. Localized new symptoms develop in some patients. Many cases require only one course of treatment, but others require two to four courses at three or four week intervals.

FEAR OF ECLAMPSIA

To the Editor:—A Negro woman aged 35 is three months pregnant. She has three living children, the youngest 9 months of age. With the last child she had severe postpartum eclampsia, her blood pressure rising well over 200. She has to work to help support the family. When first seen six weeks ago her blood pressure was 120, now it is 140 systolic and 90 diastolic, and her urine has albumin (1 plus) with a few casts. Would radical treatment including interruption of pregnancy and sterilization be justified in this type of case? Oliver A. James, M.D., Milford, Del.

ANSWER.—A blood pressure of 140 systolic and 90 diastolic associated with 1 plus reaction for albumin and a few casts in the urine is not a sufficient indication for interruption of pregnancy with or without sterilization. However, if, with satisfactory preeclampsia treatment, including bed rest, proper diet and sedatives, the blood pressure rises, the albuminuria increases and edema appears at this early stage of gestation, it is permissible to terminate the pregnancy and perform sterilization in this patient because these observations will most probably indicate that this patient has cardiovascular-renal disease. If this is so, the condition will become worse as the patient grows older. Furthermore, in cases of cardiovascular-renal disease there is a strong possibility that the baby may perish in utero or die shortly after premature labor.

CRETINISM AND PROPYLTHIOURACIL

To the Editor:—A woman aged 34, three months pregnant, has an exophthalmic goiter. Her basal metabolic rate is plus 36 per cent, her serum cholesterol level is 96 mg. per hundred cubic centimeters and her pulse rate is 104. She was taking propylthiouracil 50 mg. four times a day until her pregnancy was discovered. For fear of adverse influence on the fetus the propylthiouracil was discontinued and strong iodine solution, 10 drops three times a day, was substituted. Is there justification to fear cretinism from administering propylthiouracil to the pregnant mother? M.D., New York.

ANSWER.—There need be no fear regarding the occurrence of cretinism in this case, particularly since the amount of propylthiouracil was not excessive and was given only in the early part of pregnancy.

IMPAIRMENT OF BLOOD FLOW IN ALL LIMBS

To the Editor:—Oscillometric readings of all four extremities have been made on a man aged 35. There appears to be a definite impairment of blood flow in all four limbs, perhaps as much as 50 per cent. What condition or conditions might be responsible? M.D., Connecticut.

ANSWER.—This is an unusual situation for a man aged 35, and without additional data a diagnosis cannot be made. The first consideration is the validity of the observations. It is difficult to state the limits of "normal" oscillometric readings. Varying environmental and emotional conditions may have much influence on the so-called normal. However, granted that the readings are abnormally reduced one must first think of conditions associated with a low pulse pressure such as idiopathic hypotension, tachycardia, aortic stenosis, constrictive pericarditis and other forms of heart disease. If the pulse pressure is adequate one would have to consider premature arteriosclerosis, as in diabetes mellitus and Buerger's disease.

MILD CONJUCTIVITIS

To the Editor:—**Please discuss the prognosis and treatment of the following case: On Oct. 5, 1949 a drop from expectoration containing tubercle bacilli fell into the left eye of a man aged 28, who weighed 170 pounds (77 Kg.), and was 5 feet 11½ inches (182 cm.) tall. After cleaning the eye with water and instilling 2 drops of a 2 per cent solution of mild protein silver, this patient discontinued treatment. Mild conunctivitis developed two days later on that same eye, persisting with slight fluctuations until October 13.**

M.D., Cuba.

ANSWER.—The period of incubation for tubercle bacilli in the conjunctiva varies with concentration of the infective agent and the susceptibility of the host. It is not at all likely that the expectoration mentioned in this case contained only Mycobacterium tuberculosis as a pathogen. The irrigation of the eyes with water and instillation of 2 per cent solution of protein silver probably removed most of the foreign matter, so that serious infection of the conjunctiva from the drop of expectoration would be considered as a rare and unanticipated complication. Mild conjunctivitis that developed two days later could be considered a coincidence. However, the secretion should be carefully examined for Mycobacterium tuberculosis, and animal inoculations should be made if the conjunctivitis becomes chronic. Evanescent mild episodes of conjunctivitis can hardly be attributed to tubercle bacilli.

PREVENTION OF CREEPING ERUPTION

To the Editor:—**There are a large number of cases of larva migrans in this town. Is there a prophylactic available which could be used to spray the yards and the children's sand piles?**

A. P. Rosenfeld, M.D., Darlington, S. C.

ANSWER.—Spraying the yards and sand piles with larvacides without eliminating, or at least greatly reducing, soil pollution by infected dogs and perhaps cats will not solve the larva migrans problem. Probably creeping eruption in Darlington is due to Ancylostoma braziliense mass infection of these animals. Human infection can be controlled to a considerable degree by getting rid of tramp dogs and cats and requiring every owner of dogs and cats to administer a hook worm vermifuge to these animals and repeat treatments as required.

It would be advisable to provide new, clean sand piles for the children. These should be inspected frequently for pollution. Fences around the piles will give additional protection against contamination by dogs. The most practical way of eliminating larvae in old sand piles, surrounding soil and other areas is saturation with concentrated salt solution to a depth of at least 1 inch (2.5 cm.). All the sand in small piles should be saturated. This has been reported to be effective on some fox farms and should give good results in areas polluted by dogs.

LUPUS ERYTHEMATOSUS

To the Editor:—**I should like to know whether the discoid form of lupus erythematosus is ever associated with disseminated visceral lesions. Of the few cases of disseminated lupus erythematosus which I have seen, none have displayed the discoid type of skin lesion. However, in a patient now receiving treatment for discoid lupus there is developing a fleeting arthritic process characterized by red, slightly swollen and painful small joints but no evidence of cardiac or renal disease. It thus becomes important to decide whether these two processes should be considered coincidental or closely related.**

M.D., Illinois.

ANSWER.—Discoid lupus erythematosus usually affects the skin only. In fact, the differences between the discoid type and acute disseminated lupus erythematosus are so striking, both clinically and in the laboratory observations, that it has been suggested that the two are distinct diseases bearing no relationship to each other. However, on rare occasions cases are observed that do indicate a relationship between the two. A case of localized discoid lupus erythematosus may suddenly become disseminated with associated systemic involvement, or—though more rarely—a case of systemic disseminated lupus erythematosus, after a prolonged course, may assume the picture of discoid lupus erythematosus.

USE OF THYROID EXTRACT FOR EXOPHTHALMOS

To the Editor:—**Please give information concerning the use of thyroid extract to decrease the exophthalmos in hyperthyroidism.**

Jack Troy, M.D., Whiting, Ind.

ANSWER.—Administration of desiccated thyroid is not of value in diminishing the exophthalmos in patients with exophthalmic goiter in the hyperthyroid state. In patients in whom the exophthalmos persists after the basal metabolism has dropped to a normal or subnormal level, the administration of desiccated thyroid is sometimes of value in producing a decrease in the exophthalmos, particularly in patients who have some hypothyroidism. According to some observers, it works better if iodine is given at the same time. The amount of improvement produced by the administration of desiccated thyroid is slight, but in some patients it appears to be definite. Unfortunately, the treatment of malignant exophthalmos following a subtotal thyroidectomy or the administration of radioactive iodine and antithyroid drugs for exophthalmic goiter is not satisfactory. Recent observations indicate that ACTH may be of new value in the treatment of malignant exophthalmos.

NEUROFIBROSARCOMA OF HAND

To the Editor:—**A 41 year old white man had a mass removed from the volar aspect of the proximal end of the palm of the hand fourteen years ago. There was no recurrence until about five years ago. At the same location the mass became larger, so that preoperatively it measured about 1 inch (2.5 cm.) in diameter, and was slightly tender. There is no record of a pathologic examination of the tumor removed fourteen years ago. I excised the new mass on Jan. 31, 1949. There was much fibrous tissue reaction around it, so that possibly a portion of the capsule of the tumor remains. The pathologic diagnosis was degenerating schwannoma or neurinoma of the hand. Enclosed is a copy of the pathologic report. For the past month there has been another small nodule, about 0.5 cm. in diameter, developing at the same site. It is tender. Should I excise this again or irradiate it?**

M.D., Oklahoma.

ANSWER.—The tumor removed from the volar aspect of the palm of the hand fourteen years ago was undoubtedly a neurofibrosarcoma. This is a malignant tumor which does not metastasize but has a tendency to local recurrence if inadequately excised. This tumor grows relatively slowly. The present recurrence, after the second operation, Jan. 31, 1949, should be again excised, with reasonably wide margin compatible with good function of the hand. This tumor will not respond well to roentgen therapy.

BLOOD TEST FOR THYROID ACTIVITY

To the Editor:—**What blood test is made to determine the function of the thyroid gland? If there is such a test, what is the procedure and what are the advantages over the basal metabolism test?**

A. C. Armbruster, M.D., Phoenix, Ariz.

ANSWER.—Determination of the protein-bound iodine is used as an index of thyroid function. In certain instances the basal metabolism may be low and in other instances high when there is no abnormality of thyroid function. For example, certain patients with a low basal metabolism do not appear to have hypothyroidism. Some patients with lymphatic and myelogenous leukemia may have a high level of basal metabolism without any disturbance of thyroid function. The determination is of value primarily in patients who present a problem in diagnosis. In most instances it is not necessary to use the test for adequate clinical management of patients. The administration of desiccated thyroid or of iodine may give false high readings.

CALCIUM INTAKE DURING PREGNANCY

To the Editor:—**Is there any evidence to show that the calcium supplied by milk is preferable to calcium pills during pregnancy? What is considered the best supplementary form of calcium in the diet of the pregnant woman? Should vitamin D be given routinely with supplementary calcium?**

M.D., Indiana,

ANSWER.—There is no evidence to show that calcium supplied by milk is preferable to calcium pills taken during pregnancy. However, since milk contains many other ingredients besides calcium which are important during pregnancy, pregnant women should drink a quart of milk a day unless this is contraindicated. One of the best supplementary forms of calcium is calcium gluconate. Vitamin D should be given routinely with supplementary calcium.

BILATERAL VASOTOMY IN A YOUNG MAN

To the Editor:—**A young male patient has requested me to do a bilateral vasotomy for sterilization. Before considering the operation I would like to know what to expect in the way of after-effects. I am particularly interested in the effect it will have on the size and function of the testicle. For example, what would be the status of a man's testicle ten years after an operation when it is done on a young man? What is the effect on his potency?**

E. E. Benoist, M.D., Natchez, Miss.

ANSWER.—Vasotomy does not have any apparent effect on the size and function of the testicle ten years after operation. Potency is not affected; in fact, some men contribute the information that their potency has increased following such a procedure.

EFFECT OF BURLAP ON SKIN OF HANDS

To the Editor:—I have as patients men who handle burlap soaked in 90 per cent sodium chloride solution. Their hands become rough and the skin broken and infected. What procedure is recommended to protect their hands?

M.D., Massachusetts.

ANSWER.—Burlap bags are made from the fibers of jute. The native material is relatively free from skin irritant properties. However, in this country some burlap products and notably "battings" may represent reclaimed jute, previously treated with oils or tars, and occasionally admixed with the coarser henequen or maguey fibers. Dermatitis, either chemical or merely mechanical, from burlap material is recognized. In the present instance the brine is the more practical threat. In the form of dust, crystals or strong brines, salt is a great dehydrator. Fissured eczema is a common manifestation. This irritant is one of few that readily attacks the palms along with other portions of hand and forearm integument. The usual types of "protective creams" do not provide much protection. Chief reliance must be placed on mechanical protection such as plastic gloves or gauntlets sufficiently long and close fitting to prevent entry of salt. Leaky gloves are worse than none. Use of bland emollients before and after work is helpful but insufficient. Use of harsh detergents after exposure to brine is undesirable.

PAIRED PATCH TESTS

To the Editor:—What is the technic and clinical significance of paired patch tests?

Walter Weinberger, M.D., Altoona, Pa.

ANSWER.—Paired patch tests are applied with comparable technic to the usual patch test. The difference is that the test is performed in duplicate. For example, the proper concentration of the test solution is moistened on a cloth square, covered with cellophane and then by a standard adhesive tape covering. If the test is applied to the left shoulder, then the paired test is applied to the right shoulder; if to the left arm, the paired test is applied to the right arm.

The clinical significance of the paired patch test is that it is a far more accurate and reliable diagnostic aid than the single patch. The simultaneous duplication of a reaction (either positive or negative) conveys specific information and may be considered statistically as the equivalent of four to six standard patch tests.

KARO® CORN SYRUP AND DIABETES

To the Editor:—I have a letter in which the statement is made, "Karo Blue Label® Corn Syrup has been used in controlling 1 case (of diabetes) without insulin for eight years and 2 cases, after three years on insulin, for three years without further injections of insulin." The informant states that he controls his own diabetes without insulin by taking 1 level teaspoonful of the bulk inositol and 1 tablespoonful of refiner's syrup. Has this work been confirmed?

John H. Bohmfalk, M.D., San Antonio, Texas.

ANSWER.—A search of the literature has failed to disclose confirmation of the value of Karo Blue Label® corn syrup or inositol in controlling diabetes.

BUNIONS

To the Editor:—I would like to know the shortest period of time necessary for the development of moderate-sized bunions.

Anthony M. Puleo, M.D., Cleveland.

ANSWER.—Literally a bunion is a bursitis. An inflammation of the bursa can occur in three or four days, or less, from the wearing of a tight shoe and from excessive walking. Frequently, when one talks about bunions, the hallux valgus which is associated with the bursitis is presupposed. A longer period of time is required to develop a hallux valgus; it is a gradual process, and it would be unusual for a hallux valgus with bunion to develop in less than three months.

HARDENED EAR WAX

To the Editor:—Is the use of auralgan® (antipyrine and benzocaine in dehydrated glycerol) or any softening and germicidal oil indicated before removal of hardened ear wax?

Fred F. Prausnitz, M.D., Larchmont, N. Y.

ANSWER.—Hardened ear wax may often be removed without preliminary softening. This may be accomplished by syringing with warm water or by the use of proper forceps. The effort at all times should be to accomplish the purpose with ease and without pain or injury to the tissues. If such attempts fail, then the cerumen may be softened by agents such as hydrogen peroxide, glycerine or sodium bicarbonate solutions in glycerine.

VISIBLE CERVIX FOLLOWING DELIVERY

To the Editor:—Following delivery, if the cervical uterine os is apparent almost at the level of the internal labia, does that indicate that the cardinal ligaments have been stretched or torn beyond their normal limits?

Robert A. Heebner, M.D., Compton, Calif.

ANSWER.—Normally after delivery the cervix is high in the vagina. Therefore, it is necessary to insert a speculum or retractors to expose it. If the cervix is visible at the vaginal introitus with or without separation of the labia, the condition is abnormal. The cause is usually some fault in the supporting mechanism of the uterus, namely, in the cardinal and uterosacral ligaments. In rare instances, however, the cervix may be visible at the labia because of a true hypertrophy and elongation of the cervix. In such instances the ligaments may be intact.

GALLSTONES AND KIDNEY STONES

To the Editor:—Is there any diet or medicine which will dissolve gallstones or kidney stones?

J. M. Hesser, M.D., Benson, Ariz.

ANSWER.—There is no known means of dissolving gallstones within the body. As to kidney stones, small phosphate calculi may slowly diminish in size on an acid ash diet. Stones in the bladder or renal pelvis, if of certain chemical composition, may be dissolved by irrigating solutions, but the unpleasantness of this procedure is sufficient to make it impractical in most instances. For the ordinary types of urinary calculi which are not causing obstruction which would require surgical intervention, a low calcium diet and a high fluid intake are to be employed.

GYNECOMASTIA

To the Editor:—I excised a piece of tissue from a tumor of the right breast in a man aged 66 and the pathologist reported that it was was "gynecomastia." What treatment, if any, is indicated in such a case?

M.D., New York.

ANSWER.—If the diagnosis is gynecomastia rather than any definite tumor (circumscribed growth), it is suggested that complete removal of the affected breast is in order provided this is sufficiently large to cause embarrassment or is the source of pain. Otherwise, it does not need attention. Of course, one should search for underlying causes such as cirrhosis, radical dietary inadequacies, or the presence of any feminizing tumor, particularly in the genital tract.

PROGRESSIVE DEAFNESS

To the Editor:—A woman now aged 42, noticed that she was beginning to lose her hearing during her first pregnancy, twenty years ago. The deafness has been slowly progressing. She has consulted several otologists, without any improvement. She has heard about some "hormone therapy" for deafness and wants to know about it. I do not have the results of any otologic tests and do not know whether her deafness is of the nerve type or not. Please give me information as to hormone therapy in this condition.

Sol. M. Wolffson, M.D., Beverly Hills, Calif.

ANSWER.—Apart from the exceptional case of nerve deafness associated with myxedema, in which thyroid medication can result in appreciable improvement in hearing, there is no known effective endocrine treatment for impaired hearing. From the brief history, it is possible that this patient is suffering from otosclerosis and the possibility of the fenestration operation should be considered. She should have a complete otologic examination, including air and bone audiometry to determine this.

UNDESIRABLE EFFECTS OF PROCAINE ANESTHESIA

To the Editor:—Please advise concerning the safety and value of the intravenous injection of 1 per cent procaine in 5 per cent dextrose as an anesthetic in obstetrics.

M.D., Texas.

ANSWER.—Only limited clinical data are available on the use of procaine intravenously as an anesthetic in obstetrics. Considerable data are accumulating concerning the undesirable effects of this type of anesthesia. Sudden circulatory depression may occur and may involve decided drops in blood pressure. Respiratory arrest is not uncommon and may coincide with the circulatory depression. These serious complications are particularly undesirable in obstetrics, where they may result in fetal anoxia which may cause permanent injury or death. These and other disadvantages such as drug sensitization, delayed toxicity and technical difficulties in the administration of this form of anesthesia far outweigh any advantages that it may have in obstetrics.